ENDEAVOUR
VOL 8
1949
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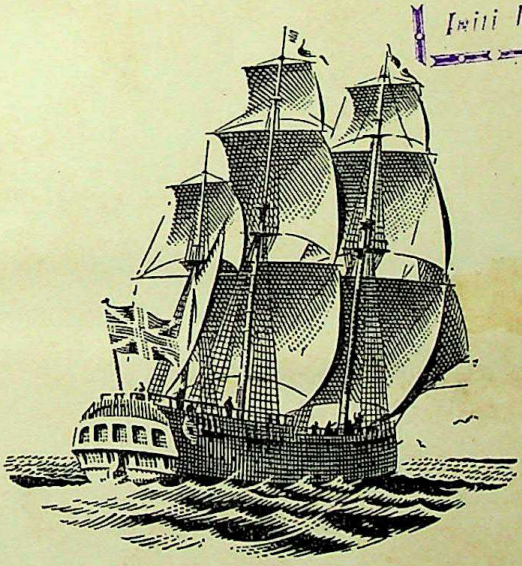
ENDEAVOUR

quarterly review designed to record the progress of the sciences in the service of mankind



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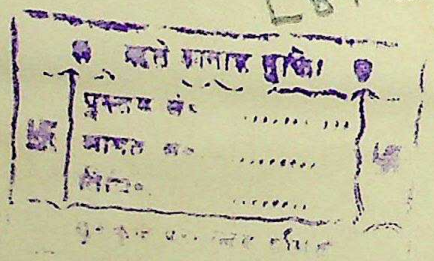

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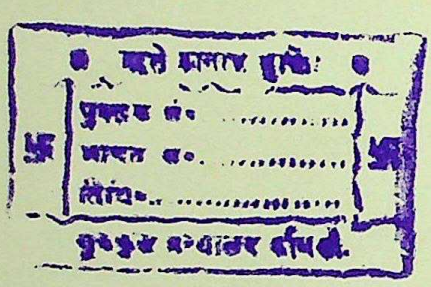

Made and printed in Great Britain at THE KYNOCH PRESS, *Witton, Birmingham, 6, for the publishers,*
IMPERIAL CHEMICAL INDUSTRIES LIMITED, *London, S.W.1*

ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

VOLUME VIII JANUARY 1949 NUMBER 29

The Philosophical Magazine

At the end of the eighteenth century the growing interest and activity in science found expression in what is an outstanding development in the history of exact knowledge, namely the foundation of journals devoted to specialized branches of science. Up to that time the various existing periodicals had dealt with the whole field of scientific endeavour, and sometimes indeed with all learning: now, the needs of those with more limited but more inquiring interests were to be met. In France appeared the *Annales de Chimie*, in Germany the *Journal der Physik* (which later became the *Annalen der Physik und Chemie*), and in England, in 1798, our renowned *Philosophical Magazine*, which has recently marked its 150th anniversary by the issue of a commemoration number devoted mainly to the history of Natural Philosophy in the eighteenth century.

Natural Philosophy was the title chosen by Newton for the book in which he inaugurated a new age in physics and astronomy; Thomas Young in 1807 called his book *Lectures on Natural Philosophy*; and in the Scottish universities physics still goes under the traditional name of natural philosophy. *The Philosophical Magazine* in the beginning reported on matters covering a wide range of interests, including chemistry, astronomy, geology, and occasionally biological subjects, but its interests were largely physical and it gradually acquired fame in civilized countries all over the world as an organ for the speedy publication of results of original research in physics.

The Philosophical Magazine, or 'Phil. Mag.,' as it is briefly—almost affectionately—termed by men of science, has an interesting history. Founded by a Scot, Alexander Tilloch, who for some obscure reason adopted this form in preference to his father's name of Tulloch, it was a private venture, and as such it has developed through its long life to the present day. Since 1827 *The Philosophical Magazine* has been printed by Taylor and Francis at an old house in Red Lion Court, in the City of London, which is a delightful surprise to him who visits it for the first time. The fine seventeenth-century staircase, with the Jacobean twisted wooden columns supporting the balustrade, leads to old rooms in which what are now capacious cupboards were installed as powdering closets in Georgian days. An atmosphere of solid and sober tradition and of good craftsmanship is appropriate for the printing of a scientific journal with its fruit in the present but its roots in the past, for which the careful hand-setting of the much-experienced compositor is necessary if the mathematical machinery of the journal is to show clear.

Looking back to those first days at Red Lion Court, the interest which the world of scientific research came to take in the publication is indicated by the fact that in 1832 David Brewster became one of the editors; he held this position until his death thirty-six years after. Later Kelvin, Lodge, and J. J. Thomson lent as editors the power of their names to promote the influence of the *Magazine*, while the support of Ireland was evidenced by the inclusion of Fitzgerald and John Joly. It is doubtful if these great men took any active part in the running of the paper, especially as they mostly lived at some distance from London, but they were available for consultation, and the presence of their names was a guarantee of the confidence felt by the scientific world in the conduct of the paper. They undoubtedly influenced many first-class workers to contribute to the *Magazine*.

What a list the contributors make! Faraday, Airy, Joule, Rowan Hamilton, Kelvin, Stokes, Rayleigh are British names that come at once to mind, while Helmholtz and Witkowski remind us that the great men of the European mainland

also sent papers. Some of the greatest American physicists, such as Rowland, published in the *Magazine*; Michelson and Morley's epoch-making paper appeared here in 1887. It was, however, the coming of the electron, of radioactivity, and of other aspects of atomic physics that ushered in the full glory of the 'Phil. Mag.' Not only did J. J. Thomson and Rutherford publish most of their papers there, but so did their collaborators and students, English and foreign. Take down those great books, Thomson's *The Conduction of Electricity Through Gases* and Rutherford's *Radioactivity*, and references to the 'Phil. Mag.' strike the eye at every turn of the page. Rutherford's first paper on the nuclear structure of the atom, Bohr's first papers on atomic structure, Moseley's announcement and development of his law, Aston's early work on isotopes—all appeared in the *Magazine*. It would be an exaggeration, but not a great exaggeration, to say that the whole of the foundations of modern atomic physics could be constructed from the papers contributed to the 'Phil. Mag.' in the thirty years from 1895 onwards.

It would be idle to pretend that *The Philosophical Magazine* enjoys at the moment the glory of the days when it was the main organ of publication of the Cambridge and Manchester schools of research, and when a great question in the laboratories of Europe and America was 'What's in the "Phil. Mag." this month?' Many factors have told against the speedy publication, at one time characteristic, which was possible in former days; the great patrons of the past are gone and their successors have other traditions and other ties; and the proceedings of the learned societies that deal with physics have increased their scope and the efficiency of their machinery for publication. There is, fortunately, little doubt that those responsible for the conduct of the *Magazine* are well apprised of the present position and are taking active steps to ensure that their paper shall resume the important part which it has played in the world of scientific communication. When the *Magazine* first appeared there was no introductory statement on the object or purposes which the editor had in mind: it was left to the reader to gather the policy of the *Magazine* from its content, and no doubt the shaping of this policy was influenced by the course of events. Similarly, at the present time there has been no pronouncement that a process of reform and melioration is in progress, but there are many signs that the proprietors have in hand a vigorous campaign for increasing the usefulness of their paper and for raising the general interest and importance of the communications. We understand that a more rigorous sifting of the contributions submitted has been initiated, and that special efforts are to be made to ensure the prompt appearance of records of really significant researches. Time will show whether papers from special fields are being particularly encouraged, a matter that clearly requires careful consideration by the editorial board. As far as tradition is concerned, at the time of the greatest splendour of the *Magazine* there was a preponderance of papers of a certain type caused by the support of the great schools of research to which reference has been made, but important papers from all branches of physics, both experimental and theoretical, appeared. A definite design will, no doubt, soon show itself. Meanwhile the format of the paper has recently been rendered more attractive, and the editorial board has been strengthened by the addition of Professor N. F. Mott, who—and this is an important step—assumes the duties of active editor. The other members of the editorial board—Sir Lawrence Bragg, Sir George Thomson, and Dr Allan Ferguson (who acted as executive editor for about ten years and did much to raise the standard of the papers)—vouch for the confidence of leaders of research and learning. We look forward with sanguine expectation to the already apparent new period of active renown for the great *Philosophical Magazine* and offer our warmest good wishes for a happy voyage towards the bicentenary.

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Mechanism of chemical reactions

MICHAEL POLANYI

The detailed nature of the mechanism of chemical change was, of course, an insoluble problem until the main principles of atomic structure had been established. During the last two decades, however, much progress has been made, chiefly on the basis of quantum mechanics. Professor Polanyi, himself one of the leading workers in the field, describes the electron-switch theory of chemical reactions and explains some of its applications.

EARLIER DEVELOPMENTS

Twenty years or so ago we already knew that the rate-constants of chemical reactions are of the form given by Arrhenius, $k = Ze^{-Q/RT}$, and the nature of the temperature-independent constant Z was fairly well understood. It meant either the number of collisions occurring per second between reacting molecules (Trautz) or—in the case of unimolecular reactions—the number of fluctuations occurring per second in the energy content of the chemical bond primarily affected by the reaction [1]. It was also clear that the factor $e^{-Q/RT}$ indicated the probability of a collision or a fluctuation overcoming an energy barrier of the height Q. But that was as far as our understanding went. We did not know what the activation energy Q really meant, or what kind of motion the atoms were supposed to be performing in surmounting the energy barrier.

QUANTUM MECHANICS

A new leaf was turned when F. London's paper appeared in 1928 [2]. Here was a principle, set out in terms of the new quantum mechanics, according to which at least the simplest chemical reaction (one free atom attacking a diatomic molecule) could be plausibly represented, and even calculated—though somewhat crudely—in detail. H. Eyring and I took up the idea and worked it out in some concrete examples [3]. It appeared to serve well enough, but the new approach seemed rather abstruse. The further development of this line of thought lay principally in the hands of Eyring and his school, whose work has been summed up in the book by Glasstone, Laidler, and Eyring, *The Theory of Rate Processes* (1941).

THE ELECTRON-SWITCH THEORY OF CHEMICAL REACTIONS

A more direct approach and one which attempts to account for the major variations of chemical reactivity was put forward by Ogg and Polanyi in 1935 [4]. Though it is limited to reactions involving the switch-over of an electron from one centre to another, it covers a wide field of the most common chemical processes. Its principle is this. Consider the spatial arrangement of the elementary particles (atoms or ions) in the initial and final states of a reaction. We shall find in both of these states that atoms coupled by a chemical bond lie closer together than atoms which are not bound together. Since in a chemical reaction there are always bonds broken and new bonds formed, there results a rearrangement of atoms to new partnerships. Atoms which lie close together will become separated, and others formerly wide apart will become close neighbours. Take the simplest case of three particles reacting according to:

$$AX + B = A + XB;$$

it involves moving X from its close association with A and linking it to B instead. Our theory pictures this process as follows. We strain the A-X bond up to a point where X has approached B so closely that it can switch over without any further supply of energy to form the X-B bond. The configuration of the particles at which the electron switch occurs is called the *transition state* of the reaction. The work done in forming the transition state is taken to represent the activation energy Q.

Such a scheme (which must, of course, be elaborated further to be of any practical use) seems directly to suggest some connection between binding strength and chemical reactivity. Suppose we think of the oxidation of a series of hydrocarbons so that A-X represents the C-H bond in the several hydrocarbons, which is to be broken by transfer of H to the oxidizing agent Ox; then we can write the process as

$$R{-}H + {\cdot}Ox = R{\cdot} + HOx$$

where R varies in a series R, R′, R″, . . . , etc. If now we find that some hydrocarbons, e.g.

*iso*butane or toluene, are much more readily oxidized than methane, we may suppose this to be due to less work being required to strain the R-H bonds undergoing oxidation in *iso*butane or toluene than those in methane. In other words we shall try to account for the observed increased reactivities in the series R-H, R′-H, R″-H, etc., by assuming a corresponding fall in the energies of the bonds R-H, R′-H, R″-H, etc.

DETERMINATION OF BOND ENERGIES

In the past ten years it has become increasingly clear that the energy required to split a bond of a particular type, say a C-H, C-OH or C-I bond, does vary to a very marked degree in different organic molecules, and, what is more, we seem to be on our way towards a widely applicable method of determining bond energies in a series of organic compounds.

The method consists in observing the rate of pyrolysis under conditions in which the rate-determining step lies in the rupture of the bond under examination. The first condition is, of course, that this bond must be the weakest in the molecule. For the method to function smoothly, however, it is also necessary that the primary process of bond rupture should be followed neither by a back reaction nor by an indefinitely progressing chain reaction. According to M. Szwarc (1947) [5], this is true for the pyrolysis of toluene. The weakest bond here is a C-H link of the methyl group; and the primary process is accordingly:

$$C_6H_5.CH_3 = C_6H_5.CH_2\cdot + H.$$

Since the H atom immediately reacts with the excess of toluene to produce either H_2 or CH_4 (followed by the formation of dibenzyl and benzene), we have here neither a back reaction nor any consecutive chain reaction, and the number of bonds primarily ruptured per second can be measured by the amount of gas obtained from the pyrolysis.

The observations on the pyrolysis of toluene recorded by Szwarc over a wide range of temperatures do in fact yield a reliable estimate for the bond energy of C-H in the methyl group. The velocity constant obtained is of the form:

$$k = 2 \times 10^{13} \times e^{-77500/RT}$$

The factor 2×10^{13} closely corresponds to the theoretically predicted number of energy fluctuations in the bond broken by pyrolysis, while the quantity 77,500 in the exponent may be taken to represent the energy of that bond in cal/mole.

Similar observations of Szwarc on the pyrolysis of propylene have yielded

$$k = 2{\cdot}5 \times 10^{13} \times e^{-78000/RT}$$

for the rate of dissociation in the methyl group [5*a*].

This reveals a very remarkable drop in the energy of a C-H bond as compared with methane. By a variety of methods (including an indirect application of pyrolysis) it has been established that the dissociation $CH_4 = CH_3 + H$ absorbs 102 kcal/mole. Thus the replacement of an H atom of methane by a phenyl group appears to reduce the C-H bond energy in the methyl group by 24·5 kcal/mole. If such great variations can be brought about in the energies of a carbon-hydrogen bond by the introduction of different substituents on the carbon, then a theory—like the one we suggested—which explains the variable reactivity of such groups by changes of bond energy may seem quite promising. It is important, therefore, to note that a wider application of the method of pyrolysis—to organic iodides, in which as a rule the C-I bond is the weakest—has been attempted with some measure of success, and that this seems to reveal quite marked reductions in bond energy consequent on the lengthening of aliphatic carbon chains and the branching of such chains at the α carbon [6].

Once the variation of energy is determined for one particular carbon link—say for a series of C-I bonds in different positions—the result can be extended by mere calorimetry to other types of carbon bonds having the same positions. Thus the exact calorimetric determination by Rossini [7] of the heats of formation of a series of alcohols R-OH, R′-OH, etc., of the corresponding hydrocarbons R-H, R′-H, etc., yields the variable substitution heats for the sequence of reactions [8]:

$$\text{R-OH} + \text{H} = \text{RH} + \text{OH},$$
$$\text{R}'\text{-OH} + \text{H} = \text{R}'\text{H} + \text{OH, etc.}$$

So if one has obtained the energies of the bonds R-H, R′-H, etc., one can now pass from these to the energies of R-OH, R′-OH, etc.

A. R. Ubbelohde [9] and H. A. Skinner, independently, have recently opened up a line of approach which promises to include in the system of calorimetrically-determined substitution heats the carbon-halogen bonds which are difficult to tackle by combustion calorimetry. Skinner and collaborators [10] determine, for example, the heats of the reactions:

$$Cd(CH_3)_2 + 2H_2O = Cd(OH)_2 + 2CH_4$$
$$\text{and } Cd(CH_3)_2 + 2I_2 = CdI_2 + 2CH_3I,$$

from which they obtain the heat of reaction:

$$CH_3I + H = CH_4 + I.$$

A systematic extension of this method might open up wide fields when combined with further advances in the pyrolytic determination of bond energies.

The results hitherto obtained have already proved that there exist wide variations in the value of these energies. We shall now look into the question of how far the variations may in fact account for the different reactivities of the respective bonds in question.

THE SODIUM FLAME REACTION

I earlier illustrated the electron-switch theory of chemical reactions by reference to a process of oxidation in which a hydrogen atom is transferred to an oxidizing agent which I denoted by Ox. In doing so I had some interesting observations in mind which were brought to my notice in research laboratories at Billingham, showing a striking parallelism between the oxidizability of a series of hydrocarbons by nitrogen dioxide and the reduction in the energies of their weakest C-H bonds as compared with the energy of the C-H bond in methane [11]. The case is of particular interest since oxidation is one of the most important chemical processes, but it has not yet been examined in sufficient detail to serve as material for the application of our theory. Pending such further development—which may soon be brought about by the studies of oxidation now progressing in Leeds under Professor M. G. Evans [12]—we must turn for the illustration of the electron-switch mechanism to the reactions of organic halides with sodium vapour.

It will help to conceive these reactions clearly if we bear in mind the experimental method by which they are observed. The diagram in figure 1 gives an outline of the apparatus. A stream of inert gas at a few millimetres pressure is made to flow through a nozzle, carrying with it a trace of sodium vapour which reacts in front of the nozzle with an excess of the organic halide. The depth is determined to which the sodium vapour penetrates into the space in front of the nozzle before its partial pressure is reduced to a level at which the sodium resonance light becomes imperceptible (that is, about 10^{-5} mm). Other things being equal, the slower the reaction the deeper will be the penetration. The partial pressures of the different organic halides required to maintain the same depth of penetration of the sodium vapour will be the inverse measures of the rates at which these halides react with sodium vapour.

The chemical process involved here may be illustrated for the case of the chlorides. It is:

$$RCl + Na = R^{\cdot} + Cl^{-}\,Na^{+}.$$

The Cl particle is released from its partnership with R and is attached to Na, while R becomes a free radical. This is an electron-switch reaction, for it involves the transfer of an electron from the sodium atom to the chlorine atom. We can see the theoretical treatment outlined in the diagram (figure 2). This illustrates the arrangement of particles in the initial, final, and transition states, and illustrates also the two alternative electronic states of the transition state. We see that in order to make the electron-switch possible it is necessary to elongate the C-Cl bond so as to allow for the increased size of the Cl^{-} ion formed by transferring an electron from Na to Cl. The energy curves demonstrate the determination of the activation energy on the assumption that the electron-switch occurs at the configuration where the energy is the same before and after the transfer of the electron. The curve on the left (1) represents the energy required to extend the R-X bond and the curve on the right (2) shows the energy of repulsion between the free radical R and the ion X^{-}. The energy of the transition state is fixed by the crossing of the two, and the activation energy Q is the height of this crossing-point taken from the energy of the initial state [4].

Calculations of the activation energy carried out on this basis have led to values close enough to those observed experimentally [13]. There is a tendency for the predicted values to come out too high, which is due to the fact that the calculation neglects

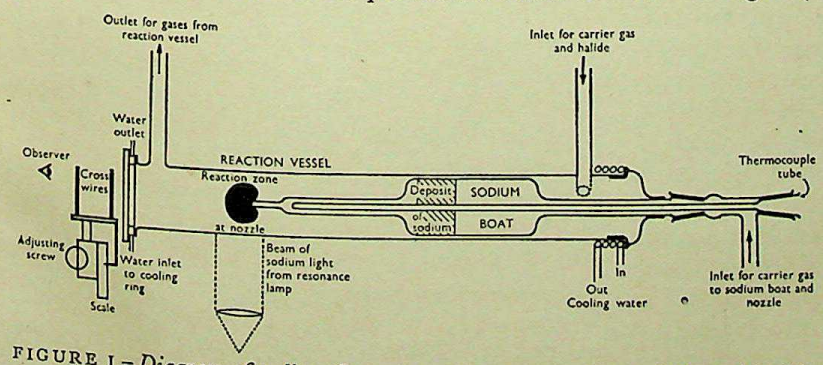

FIGURE 1 – *Diagram of sodium flame apparatus (reaction $Na + ClR \rightarrow Na^{+}Cl^{-} + R$). The observer adjusts a pair of horizontal wires to the upper and lower edges of the 'reaction zone,' the diameter of which represents the penetration of the sodium vapour into the surrounding halide.*

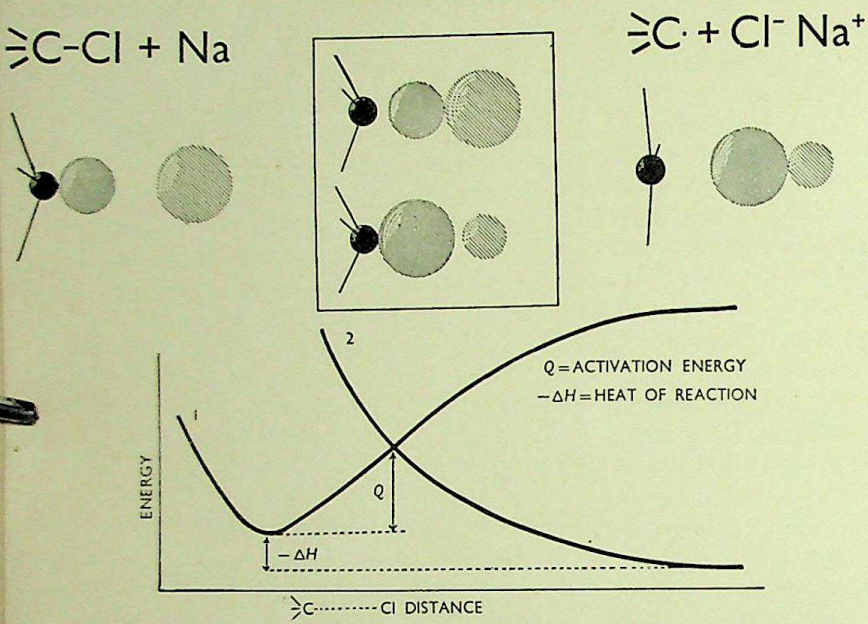

FIGURE 2 – *Theory of the activation energy of the reaction RCl + Na = R· + Cl⁻Na⁺. The 'transition state' shows two resonating configurations, before the electron-switch (above) and after the electron-switch (below). Curve 1 is the bond energy curve of R-Cl. Curve 2 is the repulsion energy curve for the particles R· and Cl⁻.*

the resonance energy possessed by the transition state in view of its two alternative electron configurations. The great simplification achieved by the electron-switch theory as compared with the more rigorous quantum mechanical theory of F. London consists precisely in taking advantage of the fact that this resonance energy can be neglected for a certain type of reaction—though the neglect is sometimes noticeable [14]. This was brought out by M. G. Evans and M. Polanyi in a paper [14] which defined the precise relation of the electron-switch theory to the theory of F. London.

Our energy diagram can be easily expanded to show more precisely how a fall in the energy of the R-X bond may be expected to reduce the activation energy and cause an increase in reactivity. This is shown for a series R-X, R′-X in figure 3. We can also express the relationship which it illustrates as a parallelism between the heats of reaction $-\Delta H$ and the rates of reaction [4, 14]. While the heats of reaction increase by the same amount by which the energies of the ruptured carbon bonds decrease, the corresponding fall in the activation energies Q appear to be only a fraction (a little over a quarter) of this decrease. That is:

$$Q - Q' = \alpha(\Delta H - \Delta H')$$
$$\alpha \sim 0{\cdot}25$$

There is a good deal of evidence to support this conclusion. If we plot the activation energies of the sodium flame reaction (as calculated from the Arrhenius equation $Q = -RT \log k/Z$) against the approximately known energies of the R-Cl bonds broken in the reaction, we find that a linear relationship of the expected kind fits the data fairly well—at least as long as we limit ourselves to compounds in which R is a pure hydrocarbon radical [6]. When R contains a negative group—for example a CO near the centre of reaction—this causes the reactivity to increase well above the value that would correspond to the bond energy R-Cl. The reason seems to lie in an increase of the resonance energy in the transition state, originating in the presence of additional electronic configurations [15]. This effect is well illustrated by recent observations of E. Warhurst and his collaborators on the sodium flame reactions of the ortho-, meta-, and para-methoxy-bromobenzenes [16]. The ortho- compound reacted three times as fast, the meta- compound 1·5 times as fast, and the para- compound at the same rate, as bromobenzene. Besides the two electronic

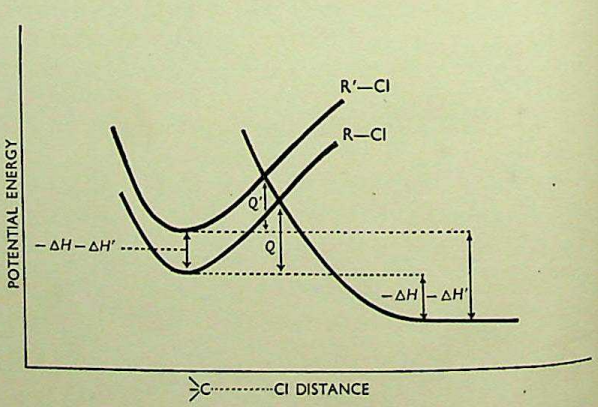

FIGURE 3 – *Illustration of the relationship $Q - Q' = \alpha(\Delta H - \Delta H')$, where $\alpha < 0{\cdot}5$. The diagram applies the derivation of the activation energy (shown in figure 2) to the case of two compounds RCl and R′Cl, the bond energies of which differ by the amount $\Delta H - \Delta H'$.*

configurations corresponding to the initial and final states, the transition state contains here the additional configuration of the type:

$$CH_3O^- \quad \cdot C_6H_4Br \quad Na^+,$$

the stability of which—and their consequent effectiveness in lowering the energy of the transition state—depends on the proximity of the two oppositely charged centres, which is greater for ortho- than for meta-, and again for meta- than for para- methoxy-bromobenzene. This accounts for the observed sequence of the reactivities of these compounds.

Before leaving the reaction between sodium vapour and the organic halides I should like to point out why it holds a peculiar and—as it would seem to me—a theoretically important position among organic reactions. It is a bimolecular gas reaction, and as such it represents the collision between two particles only. (Reactions in solution are in general complicated by the part played by the solvent.) Moreover, the theoretical treatment of the variable reactivities of the different organic radicals R, R′, etc., is greatly simplified by the fact that only three atoms have to be considered in the process: the α-carbon C, the halogen X attached to C, and the Na atom attacking X. Whatever substituents we attach to the C atom, they will affect the reaction only by modifying the C-X bond, for they are well out of the way of the attacking Na atom and do not interfere with its approach to the X atom. In other words, we can exclude in this case any steric hindrance on the part of substituents attached to the α-carbon. It also greatly simplifies the theory that the organic radical forms part of only the bond that is broken and not of the bond that is formed in the reaction. Only where this is true can the relationship hold that $Q - Q' = \alpha(\Delta H - \Delta H')$.

It is difficult to see how any other reaction could be found that is theoretically quite as simple as the sodium flame reaction.

SUBSTITUTION BY NEGATIVE IONS

The distinctive characteristics of the sodium flame reaction may become clearer by contrast if we now turn to another comparatively simple series of reactions—the more so since this series again involves the same series of organic halides. I am referring to the ionic substitution commonly exemplified by:

$$I^- + RCl = IR + Cl^-,$$

and usually carried out in solution in acetone. We may start off once more by picturing the initial and final arrangements of the reacting particles and constructing the transition state which leads from one to the other. Disregarding the molecules of the solvent, which is often permissible in this case, we may take figure 4 to represent the initial and final stages and the transition state for the case of an ionic exchange reaction:

$$I^- + RI = IR + I^-.$$

We notice that the reaction involves an optical inversion at the α-carbon (Meer and Polanyi, 1931) [17]. This was first confirmed by the study of racemization of optically active halides under the influence of the halogen ion [18]. The kinetics of this process were shown to reflect an underlying ionic exchange reaction, as represented for example by:

$$I^- + l\text{-}RI = d\text{-}IR + I^-,$$

which leads to an equilibrium mixture of the two optical antipodes. A final confirmation of the theory was given by Hughes and collaborators [19] by the use of radioactive tracers, which enabled them to determine directly the rate of the atomic exchange reaction and compare it with the rate of the accompanying process of racemization.

I have attached no energy diagram to figure 4, since in this case the energy function is too complex to be represented by a chart. We can, however, readily recognize the elements which make up the energy of the transition state. In either of the two electronic states there are present both the strain due to extension of a carbon-halogen bond and the pressure exercised by a halogen ion on the carbon centre. Some pressure will also be exercised on the substituents attached to the carbon centre, and we can foresee that if these are voluminous they might very effectively shield the

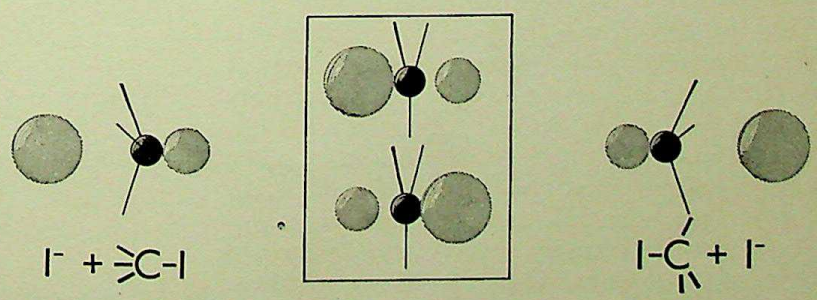

FIGURE 4 – *Configuration in the initial state and final state of the ionic exchange reaction $I^- + RI = IR + I^-$. The transition state between the two shows the configuration before the electron-switch (above) and after the electron-switch (below).*

centre from attack by an ion seeking to enter into reaction with it. Hence this type of reaction should show considerable steric hindrance by substituents attached to the α-carbon.

These factors were recognized from the start, in a general way, when the electron-switch theory of reactions was first put forward; the decisive importance of steric hindrance for reactions of the type under consideration had indeed been postulated already by Meer and Polanyi in 1931, who explained the decrease in the rate of ionic substitution in the series of the C_2H_5-, sec. C_3H_7-, tert. C_4H_9- halides by the increasing steric hindrance caused by the successive replacement of hydrogen atoms by the more voluminous methyl groups.

The theory outlined above was also used for detailed calculations of activation energies based on this theory, which were first made for atomic exchange reactions of the type $I^- + CH_3I = ICH_3 + I^-$, where steric hindrance could be disregarded [4]. The results agreed well enough with experience, though the calculated figures again tended to be somewhat in excess of those observed, which might be due to the fact that the electron-switch theory neglects the resonance energy in the transition state.

A more extensive theoretical attack on reactions of this type had to wait until methods were found of calculating the effects of steric hindrance on reaction rates. This was achieved, broadly speaking, by taking into account the van der Waals radius of substituents [20]. We may illustrate this by a picture (figure 5) showing how the methyl groups attached to the α-carbon in *tert.*-butyl chloride obstruct the approach of a Cl^- ion to the reaction centre. These groups are represented here in the way they appear in the well-known Fisher models, the atoms being enlarged on their outer side by 0·6–0·8 A as compared with their atomic radius derived from bond distances.

A recent application of these principles in detail to the known observed material has been made by A. G. Evans [21]. It is now clear that when one replaces a hydrogen atom in a methyl halide one introduces as a rule a steric hindrance to ionic substitution which greatly outweighs in its effect that of any concomitant weakening of the carbon-halogen bond, which by itself would facilitate the reaction. This is always true for the replacement of hydrogen atoms by methyl groups at the carbon centre. There are, however, at least two cases in which it does not hold. Substitution by the phenyl and the vinyl radicals can be shown to cause no marked steric hindrance, while its weakening effect on the energy of the carbon-halogen bond is known to be very large. In these cases, therefore—that is for the benzyl- and allyl-halides—ionic substitution should be much faster than for the ethyl compound, and this is confirmed by experience. The theory permits the assessment of all these effects in a semi-quantitative manner and the results are found to agree sufficiently with experience.

When we come to radicals which contain negative groups we meet a similar acceleration, due to additional resonance in the transition state, as we have seen in the case of the sodium flame reaction; the electron of the attacking ion plays here the part of the electron of the sodium atom [15]. These effects require further elucidation.

Meanwhile we may conclude that the ionic substitution of organic halides introduces one important additional factor to those which determine the rate of the sodium flame reaction, namely the steric hindrance caused by voluminous substituents on the α-carbon. The effect of this outweighs as a rule—though not invariably—the effects of changing bond energies, which dominate the sequence of reactivities in the sodium flame.

UNIMOLECULAR SOLVOLYSIS

There exists yet another type of reaction which is well suited for a systematic examination of reactivity in a series of organic compounds, and which can also be satisfactorily analysed in terms of the electron-switch mechanism of chemical reactions. It is the unimolecular solvolysis of organic halides, which was proved by Ingold and

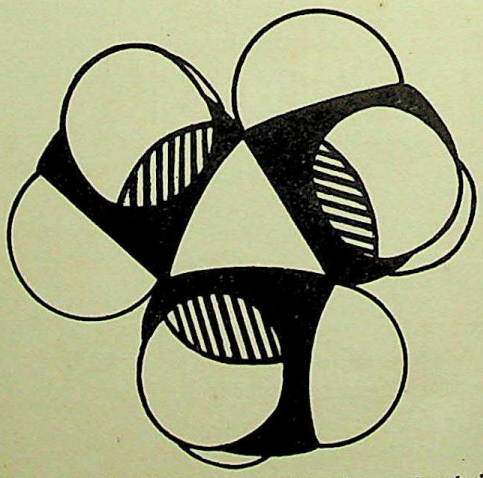

FIGURE 5 – *Model of the transition of* tert.*-butyl chloride for the reaction* $Cl^- + (CH_3)_3C.Cl = Cl.C(CH_3)_3 + Cl^-$. *The hydrogen atoms are shaded to show the penetration of the Cl particles.*

his school to be initiated and governed in its progress by an electrolytic dissociation into a positive carbonium and a negative halogen ion, $RX = R^+ + X^-$, following which the carbonium ion reacts with the solvent and forms the stable products of the solvolysis.

It is not possible in this case to draw a complete diagram of the atomic arrangement in the initial and final states, for the production of a pair of ions from a neutral pair of atoms necessarily involves a far-reaching reorganization of the solvent molecules, and we can picture only the ions, not their solvation shells. Figure 6 (top) indicates the configuration of the central particles—the α-carbon and the halogen—in the initial and final states of the primary process of unimolecular solvolysis.

We notice once more that the reaction involves an extension of the C-X bond to allow for the enlargement of the X atom when it changes into an X^- ion. The extension is somewhat lessened by the accompanying reduction of the C atom, which undergoes the loss of an electron. Much more important, however—in comparing this reaction with the two that we studied before—is the fact that the ionization at the carbon centre introduces two new magnitudes, namely the ionization energy (I) of the radical and the solvation energy (S^+) of the resultant carbonium ion.

The energy chart of this reaction can be readily outlined (see figure 6 [bottom]). The initial state is represented once more by the curve showing the energy change for the extension of the C-X bond. For the final state we have a new curve representing the energy of the two ions R^+ and Cl^- in a solvent. Where the two curves cross, the electron-switch can take place without change of energy, which according to our theory is the characteristic of the transition state, and the energy Q of the transition state—measured from the initial state—gives us the activation energy of the reaction. The diagram shows that Q does not differ appreciably from the energy of the electrolytic dissociation ED, which is also marked in the figure [23]. We shall accordingly take the magnitude of the latter to represent the value of Q.

This manner of estimating the activation energy of a unimolecular solvolysis leads quite easily to the following expression:

$$Q = D + I - E - S^- - S^+,$$

where D is the energy of the C-X bond, I the ionization potential of the radical R, E the electron affinity of the halogen X, S^- the solvation energy of the halogen ion X^-, and S^+ the solvation energy

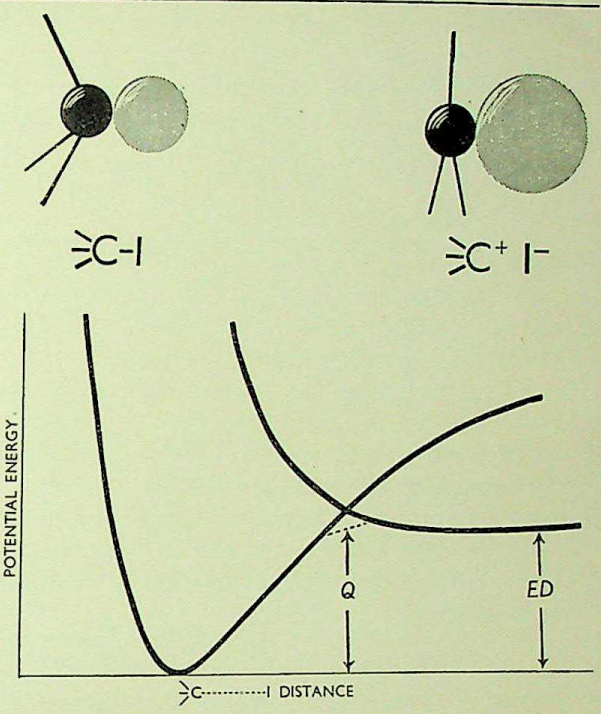

FIGURE 6 – *Illustration of the electronic reaction* $RI = R^+ + I^-$.

of the carbonium ion R^+. If we consider a series of compounds R-X, R′-X, etc., containing the same halogen atom, the variation of Q will be determined by the changes of the magnitude $D + I - S^+$.

This theory was first outlined when the electron-switch theory was originally established [4]. With the assumption, however, that the ionization potential of radicals is constant [23], which seemed justifiable at the time, it encountered great difficulties when applied to experience. It appeared, in particular, to give no explanation for the striking increase in the rate of solvolysis —to more than a millionfold—observed by Ingold in the series ethyl, *iso*propyl, *tert.*-butyl. The answer to this problem was only recently discovered by A. G. Evans [21] in the fact—which he drew from observations of American physicists [24]—that the ionization potential I of organic radicals varies over a much wider range of values than we had ever thought possible before. A. G. Evans has summarized the position in the table on page 10, which refers to the alkyl iodides with water as solvent.

UNIMOLECULAR HYDROLYSIS OF ALKYL IODIDES

In the last column is shown the predicted fall in the value of the activation energy (at absolute zero), which amounts to 63 kcal over the range of the

Radical	*D*	*I*	S^+	$(D + I - S^+)$	ΔQ
CH_3 ..	54·0	232	82	204	30
CH_2CH_3 ..	52·0	200	78	174	22
$CH(CH_3)_2$	46·5	179	74	152	11
$C(CH_3)_3$ ..	45·0	165	69	141	

whole series. In spite of the approximate nature of these calculations it is clear that they offer a satisfactory explanation of the great increase in the rate of solvolysis which accompanies the attachment of methyl groups to the α-carbon. This effect appears as due to a fall in the ionization potential from 232 to 165 kcal/mole. We may note the opposing effect of the fall in S^+, the solvation energy of the carbonium ion, which is due to the shielding effect of the voluminous substituents at the α-carbon and thus represents a kind of steric hindrance.

GENERAL CONCLUSIONS

The activation energies of the three reactions which we have surveyed in turn thus appear to be determined by an increasing number of parameters. For the sodium flame reactions Q depended (in simple cases) mainly on the energy of the R-X bond. For the ionic substitution reaction we had to add steric hindrance as a second powerful factor. And lastly, for the unimolecular solvolysis, we have to consider also changes in the ionization potential of the radical R.

Thus even for our selected group of simplest reactions we seem to be facing many complications, but this much I think may be claimed nevertheless: that the broad principles governing the mechanism of chemical reactions have become clearly visible, and that it seems possible to account in an approximate manner for the observed rate of a number of different reactions.

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[12] Based on public lectures of Professor M. G. EVANS, the substance of which I understand is in the course of publication.

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Captain James Cook, R.N., F.R.S.

SIR MAURICE HOLMES

Captain James Cook, after whose celebrated bark *Endeavour* this journal is named, charted much of the Pacific Ocean, Australia, and New Zealand, and originated scientific marine surveying. Sir Maurice Holmes here describes the main events of the great navigator's life. The painting of the *Endeavour* by Commander R. Langmaid, R.N. (retd.), from which the plate on page 14 is reproduced, is based on a contemporary drawing and on all available authentic data, and is probably the most accurate representation of the bark ever made.

James Cook furnishes a notable example of the fact that a sound constitution, a stout heart, and steady nerves are ample compensation for the accident of lowly birth. His father was an agricultural labourer, employed at the time of James's birth—27th October, 1728—at Marton, near Middlesbrough. Here James learned his letters, and on his father's transference as bailiff to a farm near Great Ayton attended the local school, where he mastered the three R's. In 1745 he went as shop-boy in a grocer's shop at the seaside village of Staithes, kept by a Mr Saunderson. Here he was drawn by the lure of the sea and was apprenticed to a Mr Walker, coal-shipper of Whitby. His experience gained during the next eight years, together with the study of Euclid and elementary navigation in his master's house when his ship was not at sea, was to prove of great value in later years.

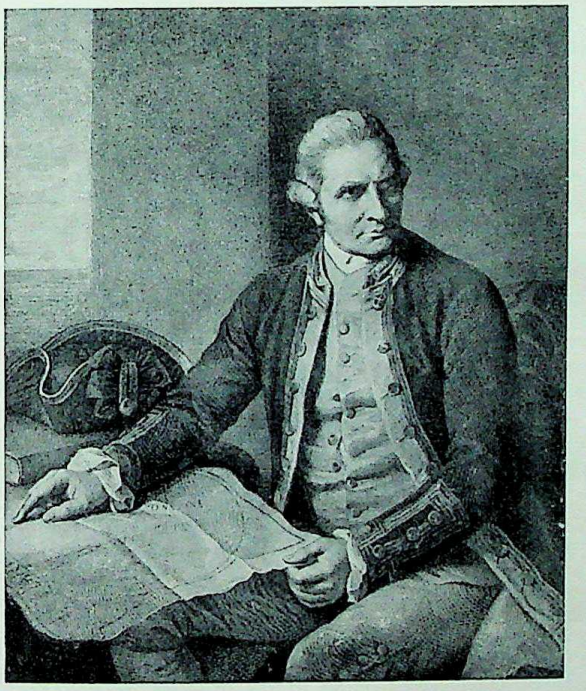


FIGURE 1 – *Engraving of James Cook by Sherwin, after a painting by N. Dance. David Sambwell* (Narrative of the Death of Captain James Cook, 1786) *says that this is an excellent likeness and, indeed, the only portrait which bears any resemblance to him.*

In 1755 Cook was offered the command of Mr Walker's latest ship, but declined it and volunteered into the Royal Navy as an able-bodied seaman, having, as he afterwards said, 'a mind to try my fortune that way.' His first ship was the *Eagle*, and, soon after he joined, the command was given to Captain (later Sir Hugh) Palliser, who was destined to have a great influence on Cook's career and to become his close friend. Cook's service in the *Eagle* coincided with the opening years of the Seven Years' War. After two years, during which he saw a certain amount of action, Cook was promoted to the *Pembroke* as Master, and sailed for Louisburg for the attack on French Canada. This gave him the opportunity for his first hydrographical experiment, the surveying of the St. Lawrence, a task so brilliantly accomplished that he received a special grant of £50. This led, after Cook's return to England, to further work of a similar kind.

Thus we find him in 1763 engaged on the coastal survey of Newfoundland, and here he was joined in the following year by Palliser, who was appointed Governor of the island. For the next four years his life followed the same pattern, the winter being spent in England and the rest of the year in Newfoundland. But during this period there was one incident which had a profound effect on Cook's future career. In 1766 an observation by him of an eclipse of the sun taken near Cape Ray was communicated to the Royal Society and published in their *Transactions*. Two years later the fruits of that incident and of Cook's long apprenticeship as a marine surveyor became apparent. In 1768 he set out on his first voyage round the world.

FIGURE 2.—Resolution and Discovery in Queen Charlotte Sound, New Zealand. From an aquatint by Piringer after J. Cleveley.

FIGURE 2.—Resolution and Discovery in Queen Charlotte Sound, New Zealand. From an aquatint by Piringer after J. Cleevely.

FIGURE 4 – Endeavour. *From an imaginative study made for this article by R. Langmaid and based upon all available authentic data.*

FIRST VOYAGE, 1768–71

The motives which underlay Cook's first circumnavigation were partly scientific, partly geographical, and partly imperialistic. It was known that in 1769 there would be a transit of Venus, accurate observation of which would determine the earth's distance from the sun, and that a similar opportunity would not recur for over a century. The Royal Society accordingly petitioned the King for a grant-in-aid of £4,000 towards the expense of sending out an expedition to an appropriate spot from which the necessary observation could be made. This proposal accorded well with the views of the Government, who were anxious to dispose once and for all of the theory, dear to the hearts of many armchair geographers, that there must be an unknown Southern Continent to counterbalance the known mass of land north of the Equator, and who were even more anxious to secure that, if there were new lands to discover and annex, they should fall to Great Britain and not to France.

The Royal Society's memorial was accordingly well received and the necessary financial provision was granted. The next question was who should command the expedition. The essential qualifications were that the commander should be a naval officer, that he should be an expert marine surveyor, and that he should have some knowledge of astronomy. Cook alone completely filled the bill, and on 25th May, 1768, through Palliser's recommendation, he was given command of the expedition with the rank of First Lieutenant. The choice of a ship was left largely to him, and, realizing the need for a ship which could take the ground and be laid on shore for repair, he chose a type with which he was very familiar, viz. a Whitby collier—a ship which was to achieve immortality as the *Endeavour*.

Cook's instructions, in a nutshell, were to observe the transit at Tahiti, then to sail south to the latitude of 40° and search for the Southern Continent between that latitude and 35° until he found it or fell in with New Zealand, a tiny portion of the South Island of which had been charted by Tasman. If the Continent were not discovered he was to explore the coast of New Zealand and return home via the Cape or Cape Horn. With the consent of the natives he was to take possession of unexplored countries in the King's name.

On 25th August, 1768, Cook set sail, accompanied, among others, by Green the astronomer and young Joseph Banks, who was in later life to be president of the Royal Society for many years. The transit was duly observed by Cook and Green independently, and, after discovering and charting the Society Islands to the westward, Cook sailed south. Finding no signs of a continent he made for New Zealand, which, in the opinion of some theorists, constituted a tip of the Continent. This theory was exploded by a complete circumnavigation of both islands.

Cook was now due to sail home either by the Cape or Cape Horn, but, acting on a discretion which his instructions permitted, he decided to steer westward until he fell in with the hitherto unexplored east coast of Australia and follow it northward. Had he foreseen the appalling perils of that journey, sometimes inside and sometimes outside the Great Barrier Reef, and his providential escape from shipwreck when the *Endeavour* grounded, he might well have chosen otherwise. As it was, after landing at Botany Bay he pursued his course northward, took possession of the east coast of Australia, confirmed the doubtful point of the separation of Australia from New Guinea, and reached Batavia. Here malaria and dysentery took their toll, and the *Endeavour* reached England with a sadly reduced company.

Cook had done all, and more than all, that he had been told to do. He had observed the transit, charted New Zealand, and demonstrated that the Southern Continent, if it existed at all, was much less extensive than its protagonists claimed. In addition, he had charted the east coast of Australia and confirmed the existence of Torres Strait.

SECOND VOYAGE, 1772–5

Although, as has been shown, Cook had administered a severe shock to the continent-mongers, he had not wholly disposed of their thesis. They contended that land in the South Atlantic which Bouvet de Lozier had sighted in foggy weather in 1739 might well be part of the Continent. This land was placed by Bouvet in lat. 54° 00′S, long. 11° 20′E. and named Cape Circumcision. Cook's instructions were to proceed by way of the Cape to Cape Circumcision and ascertain whether it was part of the Continent, and, if it was, to explore it and take possession of it. If it proved to be an island, or if he could not find it, he was to go as far south as possible and, turning eastward, circumnavigate the globe in the highest possible southern latitude.

Remembering the hazards of his first voyage, Cook would not trust himself to a single ship, and

chose two Whitby ships, the *Resolution* and the *Adventure* (Captain Furneaux). Two naturalists, father and son, named Forster, and two astronomers, Wales and Bayly, accompanied the expedition.

The ships set sail on 13th July, 1772, and after leaving the Cape on 22nd November Cook began a long and laborious search for Cape Circumcision. Having concluded that, whether it existed or not, it could not be part of a continent, Cook turned eastward and began his circumnavigation. On 17th January, 1773, he made the first crossing in history of the Antarctic Circle, and continued eastwards until he had covered more than a third of the earth's circumference. The dangers from ice and fog were almost perpetual, and it is not surprising that the ships parted company, at first temporarily and ultimately for good. After Cook had been driven northward to Queen Charlotte Sound by the season of the year and the need for a refit, he set out to complete his task, and, as an examination of the chart of this voyage will show, succeeded in doing what he had been told to do by sailing round the world in the highest possible southern latitude. It is true that he did not discover Cape Circumcision, but that was because Bouvet had seriously misplaced it in his chart. Now known as Bouvet Island, it lies in lat. 54° 26′S, long. 3° 24′E. He discovered no Southern Continent because such a continent, with its reputed 50 million inhabitants and great riches, does not exist—though had he been able to sail a hundred miles still farther south he would have found the unpeopled desert of Antarctica.

The failure to find the Southern Continent was compensated for in Cook's mind by his complete conquest of scurvy, a feat which, he wrote, 'will make this Voyage remarkable in the opinion of every benevolent person, when the disputes about a Southern Continent shall have ceased to engage the attention, and to divide the judgment of philosophers.' In his paper on the subject, which earned him the Copley medal of the Royal Society, Cook described his methods. Briefly, they consisted of insistence on the regular use of anti-scorbutics and the cleanliness of his men's bodies and clothing, the ventilation of his ships, taking on fresh water wherever possible, and keeping the men fully employed.

Soon after his return Cook was promoted post-captain and given a sinecure as one of the captains of Greenwich Hospital, with an official residence and £200 a year. However, a leisured and dignified retirement was not to be his lot.

THIRD VOYAGE, 1776–80

Having finally disposed of one age-long theory, the Great Southern Continent, the Admiralty was anxious to dispose of another which had long exercised the minds of geographers and explorers, namely the existence of a northern sea-passage connecting the Pacific with the Atlantic. Such a route, if it existed, would be very much shorter than the alternative one round Cape Horn or through the Straits of Magellan. The Admiralty felt it hardly fair to invite Cook to command the expedition, but on hearing of the project he immediately volunteered to do so. The ships were again Whitby-built: the *Resolution* in which he had sailed in the previous voyage, and the *Discovery* (Captain Clerke).

Cook's instructions, in brief, were to sail via the Cape to Tahiti, and after repatriating, either there or at the Society Islands, a native called Omai whom Furneaux had brought home with him on the second voyage, to make for the west coast of America in about 45° N and then press on to 65°, where he was to begin his search for a passage running towards Hudson Bay or Baffin Bay. If unsuccessful he was to winter in Kamchatka, and in the next year to try again farther north for a north-west passage to the Atlantic, or failing this, a north-east passage round Siberia and northern Russia.

The *Resolution* sailed on 12th July, 1776, and the *Discovery* on 1st August. On arrival at Tahiti Cook decided that Omai would be happier in one of the Society Islands and deposited him at Huahine. He then pressed northward, and on 18th January, 1778, sighted the first of a group of islands which he named the Sandwich Islands. In March he anchored in Nootka Sound without realizing the insularity of Vancouver. Keeping a close watch as he sailed northward for any opening in the coastline that might develop into a channel, he tried the only one he found (Cook Inlet) without success, and the ships made for Bering Strait, where they anchored in August.

Owing to the lateness of the season, further search for the passage had to be deferred, and Cook decided to make for the Sandwich Islands. On 30th November he sighted a new island, Hawaii, by far the largest of the group. After charting it he anchored in Kealakekua Bay. Here, owing to the supposition of the natives that he was a reincarnation of one of their gods, he was treated with adoration, and all possible supplies were forthcoming. In February, 1779, Cook left the island to resume his task. A few days later the

Resolution sprung her top-mast, and Cook decided to return to Kealakekua Bay. The natives, who had been almost eaten out of hearth and home, were less friendly, and on the night of 13th February the *Discovery's* cutter was stolen. Cook decided on a stratagem which he had often adopted in cases of theft: he would induce the king to come aboard and hold him hostage until the cutter was restored. The king made no demur, but his people did their best to dissuade him. While he was hesitating, news came that a chief had been killed while trying to escape from the bay in a canoe. Pandemonium followed and the natives set upon the escort of marines. Cook they did not dare to attack while he faced them, but when he turned to call upon the boats to cease fire he was fatally stabbed in the back.

This last voyage failed of its purpose—a failure to achieve the impossible—but, by way of compensation, the North Pacific and the Sandwich Islands found their places on the map.

Cook's contributions to the sum of human knowledge were so striking, and the fields which they covered so wide, that any attempt to summarize them must be inadequate. On the geographical side he drew back the curtain which shrouded the Pacific and disposed, once and for all, of the supposed Great Southern Continent, giving us in its place the east coastline of Australia, the map of New Zealand in all essentials as we know it today, the first vision of the Antarctic Circle, and the Sandwich Islands.

Despite his inadequate schooling he acquired, through private study in his leisure time, a considerable knowledge of mathematics, astronomy, and other branches of science, and he had a natural skill in draughtsmanship. He possessed the true scientific outlook; to be of service to geography, navigation, and other sciences was always his aim. Although astronomers were appointed to accompany his expeditions, Cook himself took the lead in the various observations of an astronomical kind made in the course of his voyages. His early observation of the eclipse of the sun in 1766 was used for the practical purpose of fixing the longitude of the place of observation.

The latitudes and longitudes of the places he visited were carefully determined by astronomical observations. On the second and third voyages he had with him the Larcum Kendall copy of Harrison's timepiece No. 4, and in several places in his journal he wrote with high appreciation of 'our never failing guide, the watch.' His positions were of a higher accuracy than had been attained by earlier navigators. Many gross errors in the positions of various places were found, and great improvements were made in the maps of the regions he visited.

Cook was, as various hydrographers to the Royal Navy have testified, the originator of scientific marine surveying. Coastlines were accurately delineated, numerous soundings were made, and the correct draughts of channels were determined. His charts were unsurpassed in his time for their accuracy and excellence. Many determinations of the variation of the compass were made, and the nature of the tides in various regions was studied and recorded. On his voyages to the far south, the Aurora Australis was observed. His conquest of scurvy and the proof that this scourge, with its appalling death-roll, was not a necessary concomitant of prolonged sea voyages, was not the least of his achievements. He was elected a Fellow of the Royal Society in 1776.

The secret of Cook's success lay in his complete singleness of purpose and his infinite capacity for taking pains. In the words of the motto embodied in his coat of arms, *Nil intentatum reliquit.* These are not spectacular attributes, but they were precisely those needed for his tasks, and they accord well with the names of his ships—*Endeavour*, *Resolution*, *Adventure*, and *Discovery*.

Leaf shape and physiological age

ERIC ASHBY

Professor Ashby observes that the change in shape from leaf to leaf on a stem raises four major problems: how shape is determined by local differences in cell division and growth; the chemical and physical background to these differences; the mechanisms by which environment affects leaf shape; and whether leaf shape is related to maturity. In the present article the last two of these problems are discussed and illustrated. Modern techniques show promise of ultimately revealing the basic causes and significance of leaf shape.

Ever since Theophrastus described the variation in shape of ivy leaves[1] there have been records of observations and speculations on leaf shape. Ruskin marvelled at its variety, 'never the same from footstalk to blossom.' Lord Avebury felt it necessary to warn his readers against 'the widely prevalent idea that the variety of leaves is a beneficent arrangement made specially with reference to the enjoyment and delight of man.' Botanists at the close of the nineteenth century believed that the ontogeny of leaf shape in individuals recapitulated the phylogeny of leaf shape in the taxonomic groups to which the individuals belonged. At the turn of the century all these comprehensive generalizations had evaporated, and modern botanists have inherited a mass of observations about leaf shape, not co-ordinated by any satisfactory hypothesis.

Recently there has been a notable revival of interest in the problems of plant morphology. The determination of shape and pattern in plants is now being studied with the techniques of genetics and physiology. One aspect of this revival, namely the study of morphogenesis at the meristems of ferns, has already been discussed in this journal.[2] The present article describes another aspect, namely the modern approach to the analysis of leaf shape in flowering plants.

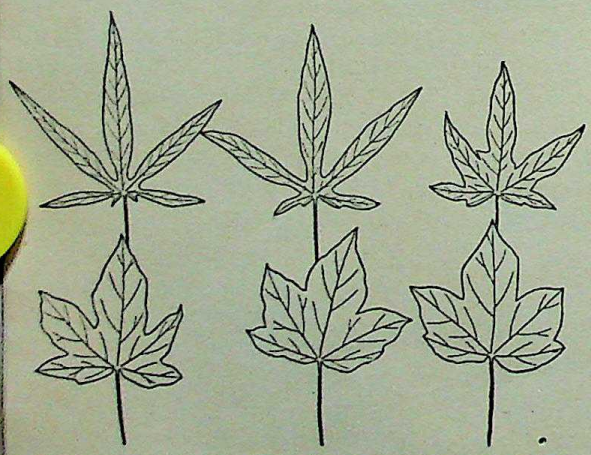


FIGURE 1 – *Leaves of six different strains of the Asiatic cotton* Gossypium arboreum. *Each shape is controlled by a specific gene.* (*From D. Hammond,* American Journal of Botany, *by permission of the publishers.*)

It is common knowledge that the shapes of leaves vary not only between varieties, but also on one and the same plant. Differences in leaf shape between varieties are due to gene differences. In the Asiatic cotton, *Gossypium arboreum*, for instance, there are at least six alternative leaf shapes (figure 1), each controlled by a specific gene. To say that leaf shape is controlled by genes does not, of course, contribute much to its analysis; the mechanism of gene action is not understood, and the problem of how genes act on leaf shape cannot be solved without solving the problem of gene action in general. In the initial stages of the analysis of leaf shape it is desirable, therefore, to exclude genetic variations, and to study only the variation of leaf shape on one and the same plant.

Observation of the shoots of flowering plants reveals the fact that successive leaves on a stem are not alike. Although all leaves begin as 'mounds' of dividing cells (figure 6), yet each adult leaf differs in shape from the leaf below it. The differences are not haphazard: they follow a consistent trend from node to node. The trend may be an increase in the amount of segmentation (as in the delphinium, figure 8*a*) or an increase in the amount of lobing (as in morning glory, figure 8*b*), or it may be a change in the relative lengths of leaf blade and petiole, together with a change in the angle between the leaf base and the petiole (as in sugar beet, figure 8*c*). These trends can be expressed quantitatively by plotting an appropriate measure of leaf shape against the

[1] *Inquiry into Plants*, i, x.

[2] ENDEAVOUR, v, 17, 1946.

FIGURE 2 – *Common harebell.*
(a) *Normal plant with juvenile and adult foliage.*
(b) *Plant grown in shade.*
(c) *Plant from cutting.*
(*From a drawing by E. H. Roberts.*)

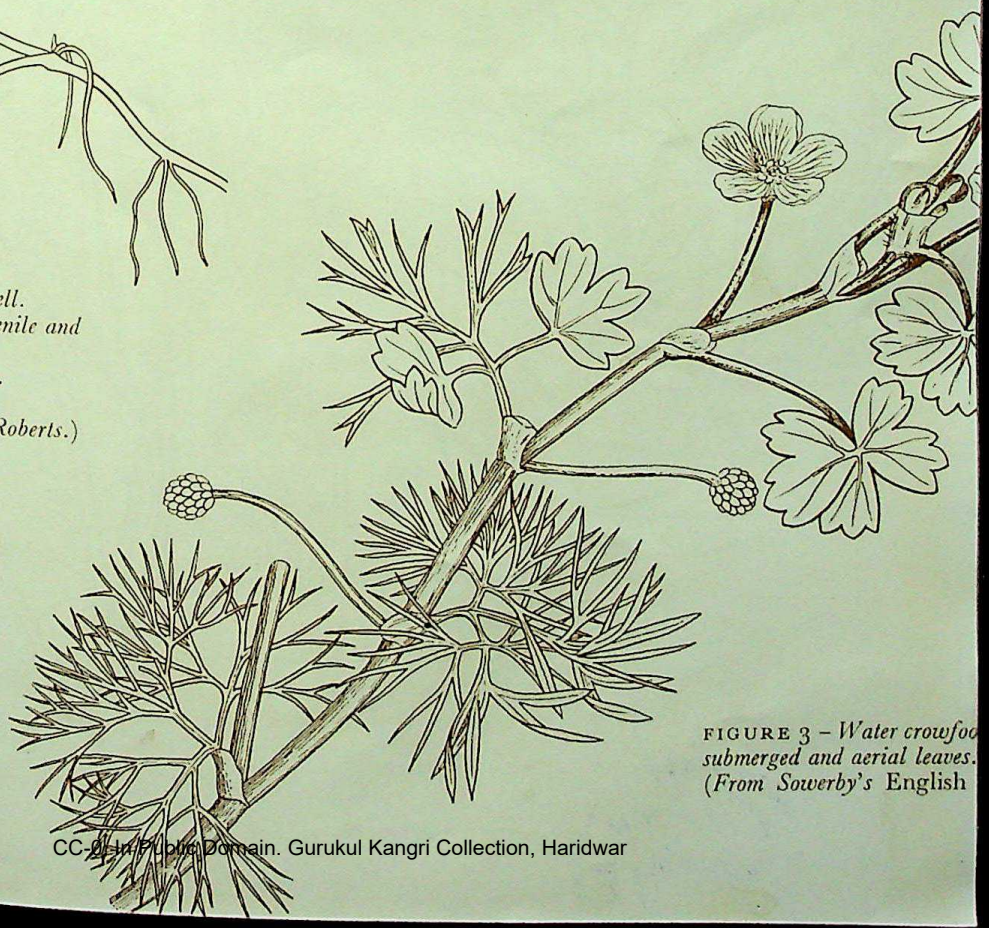


FIGURE 3 – *Water crowfoo*
submerged and aerial leaves.
(*From Sowerby's* English

FIGURE 4 – Eucalyptus Macarthuri, *showing juvenile leaves (left) and adult leaves (right). (From Baker and Smith,* A Research on the Eucalypts and their Essential Oils.)

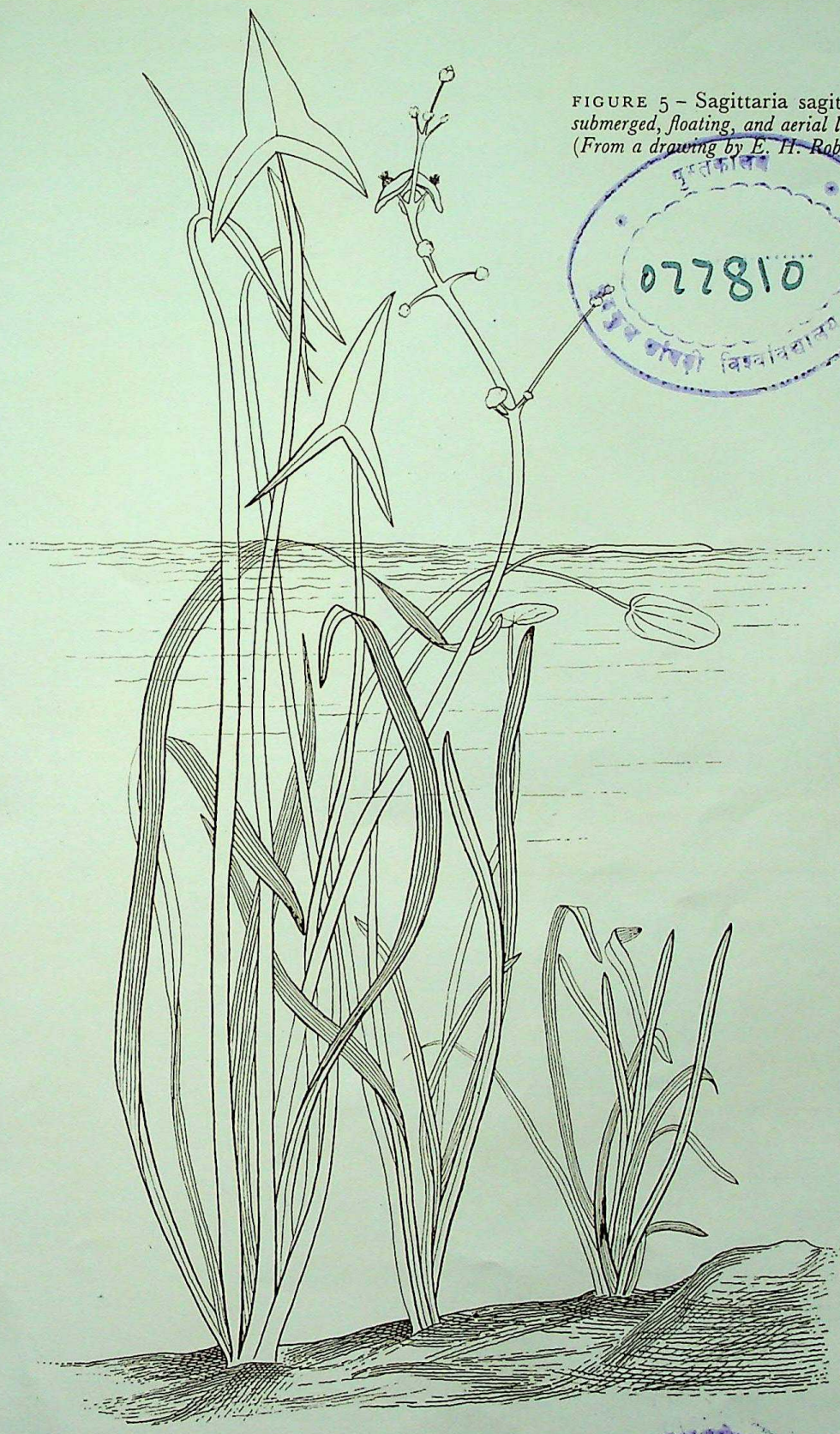
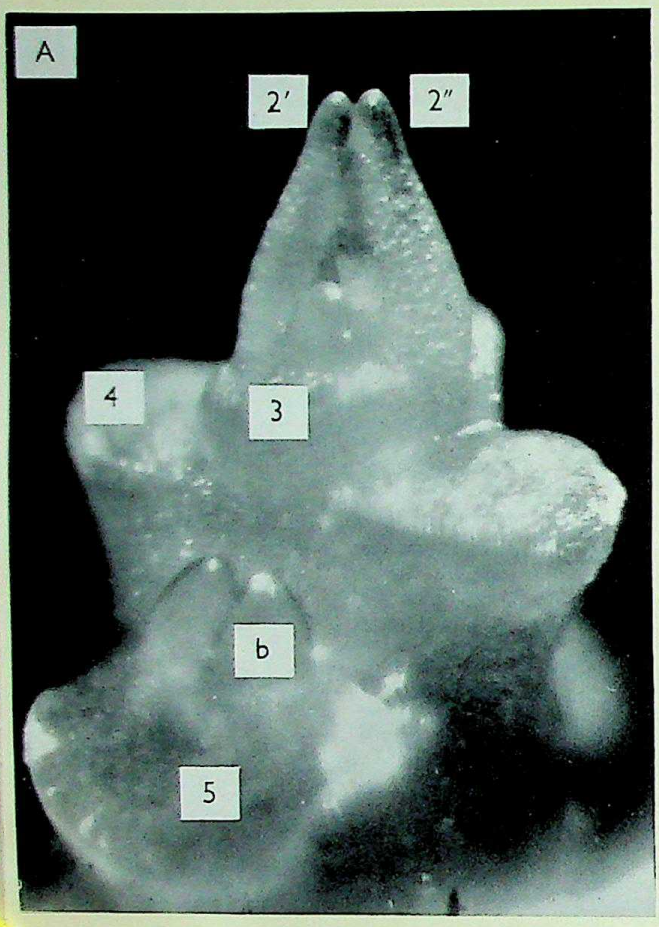


FIGURE 5 – Sagittaria sagittifolia *with submerged, floating, and aerial leaves. (From a drawing by E. H. Roberts.)*



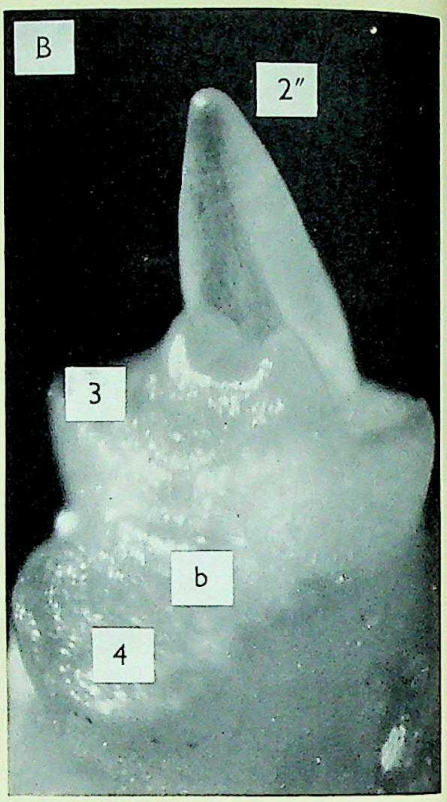


FIGURE 6 – *Early stages in leaf development. Microphotographs of apex of privet.* (A) *The third, fourth, and fifth leaves have been removed. The second pair of leaves* (2′, 2″) *is visible and, between them, one leaf of the first pair. At* b *are the first two leaves of a lateral bud.* (B) *One of the second leaves* (2″) *and the first pair of leaves.* (*Photograph by Dr B. C. Sharman.*)

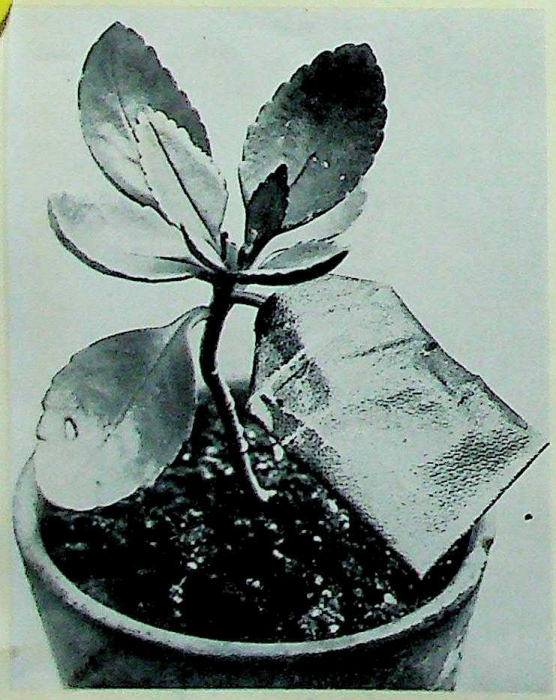


FIGURE 7 – Kalanchoe Blossfeldiana, *with one leaf subjected to nine-hour days. The treated leaf produces a substance which affects the shape of other leaves.* (*Photograph by Ernest Ashby.*)

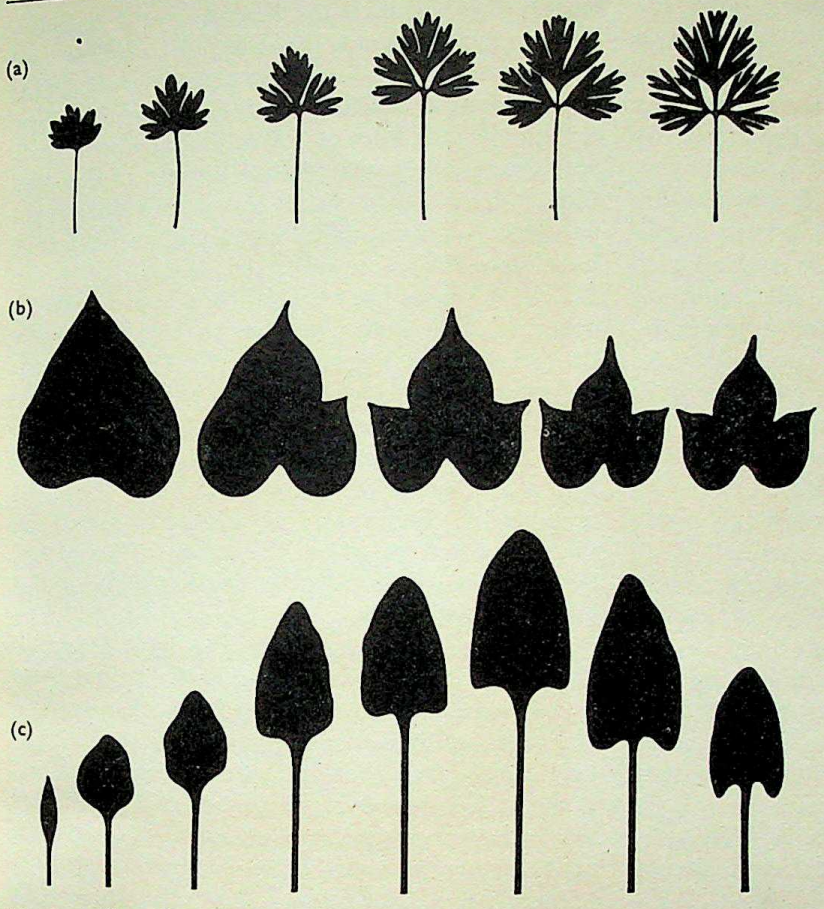


FIGURE 8 – *Successive leaves of* (a) Delphinium ajacis, (b) *morning glory,* (c) *sugar beet.* (*By permission of the Cambridge University Press.*)

number of the node at which the leaf occurs. Here, therefore, is suitable material for the study of pattern in plants—material which varies regularly and quantitatively in genetically homogeneous tissues.

A study of the change in shape from leaf to leaf on a stem raises four major problems. How is shape determined (as it must be) by local differences in cell division and growth? What is the chemical and physical background to these local differences in cell division and growth? By what mechanisms does the environment affect leaf shape? Is leaf shape related to maturity and, if so, can it be used as a measure of physiological age in flowering plants?

There is no prospect of an early solution to any of these four problems, but preliminary results are encouraging enough to justify further work. In the compass of this article only two of the problems will be discussed: the relation of leaf shape to environment, and the relation of leaf shape to physiological age.

The harebell, *Campanula rotundifolia*, has round leaves when young and linear leaves when older (figure 2*a*). Forty years ago Goebel, in Munich, cultivated harebells in very low light intensity and found that they continued to produce juvenile round leaves, even up to the flowering stage (figure 2*b*). This led him to suggest that the linear form of leaf is a response to good nutritive conditions and the round form a response to poor nutritive conditions. In good light Goebel could always produce linear leaves in succession to round leaves, but he failed by any treatment to suppress round leaves while the plant was young. He therefore concluded that the familiar youth-forms of leaves are a reflection of the initially low concentrations of nutrients in young plants. Goebel found that other treatments which deplete the nutrient reserves may evoke round leaves, even in old plants; cuttings, for instance, taken from an adult shoot which bears long leaves, very often revert to round leaves at the beginning of their growth (figure 2*c*). These reactions are not peculiar to the harebell. Juvenile leaves in other plants (for instance in eucalyptus, figure 4) can be evoked by heavy pruning or by cultivation in deep shade. Around these phenomena there grew up the tentative hypothesis that leaf form in many plants responds to nutrition, and in particular to the balance of carbohydrate and mineral salts. It was believed that if carbohydrate is depleted the primitive youth form of leaf is laid down at the meristem. This hypothesis was consistent with the behaviour of some amphibious plants. Certain water buttercups, for instance, produce one sort of leaf in water and another sort in air (figure 3). There is evidence that this response of leaf shape is not due to the air or water medium *per se* but to the fact that the leaf assimilates less efficiently in water than in air. With a high light intensity and a low temperature it is possible to produce air leaves under water, and some workers claim to have produced water leaves in air, the air being damp and free from carbon dioxide.

Similar results have been obtained using the arrowhead, *Sagittaria sagittifolia*. This plant is common in waterways in England. Its first leaves in spring are ribbon-like. These are followed by ovate floating leaves, and later in the season by arrow-like aerial leaves (figure 5). A plant cultivated in deep shade and at a high temperature continues to produce ribbon-like leaves indefinitely, even if the plant is scarcely covered with water. A plant cultivated in normal conditions produces its floating and aerial leaves at the growing-point, which may be one or two feet under water. Leaves dissected from the growing-point in summer, even when they are very small, already have the shape of adult aerial leaves. Leaf shape is clearly not a response to water level, but it may reasonably be regarded as a response to changing nutrient level during the growth season.

This familiar behaviour of water plants cannot, however, be extrapolated to explain the leaf-to-leaf trends in shape among many land plants. Changes of shape of the sort shown in figure 8 take place irrespective of gross nutrient level or light intensity. However, there is recent evidence that it is not the gross nutrient level but the presence of specific growth-form substances which controls the trend in leaf shape in certain plants. At Göttingen, during the last eight years, Harder and his colleagues have studied the flowering and morphology of the succulents *Kalanchoë Blossfeldiana* and *Sedum kamschatkicum*. In these plants they find that both flowering and the gradual change in shape and succulence from leaf to leaf through the year are controlled by the relative lengths of day and night. Even when a leaf is already partly expanded, a change in the length of day will change its shape. Harder subjected single leaves on *Kalanchoë* plants to artificial nine-hour days by covering them from 5.30 p.m. to 8.30 a.m. every day with black bags (figure 7). Following this treatment the next leaf vertically above the treated leaf assumed a 'short-day shape.' Harder interprets this as evidence that short days produce in a leaf some formative substance, which he calls metaplasin. This substance is able to diffuse up the plant and to affect the shape of immature leaves above, even though they are living under long-day conditions.

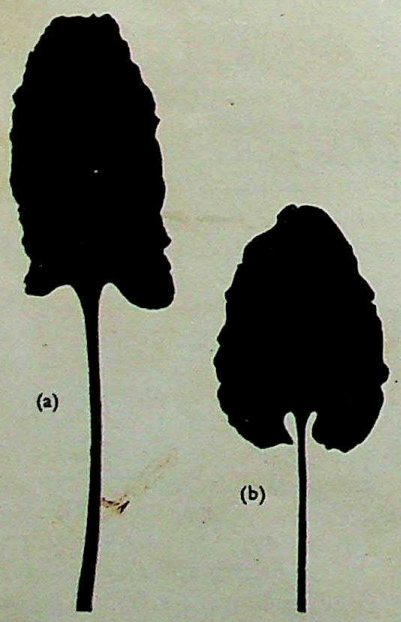


FIGURE 9 – *Sixteenth leaves of sugar beet:* (a) *heavily irrigated,* (b) *unirrigated. Both leaves are about the same time-age.* (*From Minina,* Theory of Cyclic Ageing and Rejuvenescence, *Moscow.*)

The discovery that leaf shape in *Kalanchoë* is dependent on the relative lengths of day and night is consistent with observations from other sources. In cotton (*Gossypium herbaceum*), for example, it has been established that the rate of change of leaf shape is influenced by length of day. The first leaves in some varieties are entire, and the amount of dissection increases from leaf to leaf until a 'climax' type of leaf is reached, which may be very deeply dissected. The time of flowering usually corresponds with the appearance of the climax type of leaf. In varieties with dissected leaves there is a clear connection between the development of dissection at an early node and early flowering: cultural conditions which hasten the one also hasten the other. The number of nodes which bear juvenile leaves is correlated with the duration of the preflowering period of development.

This evident parallelism which has been observed in cotton between the rate of change of leaf shape from node to node and the rate at which sexual maturity is reached led a Russian botanist, N. P. Krenke, to suggest that change in shape of successive leaves might be used to measure physiological age. Physiological age is a familiar but elusive concept in biology. The saying that a man is as old as he feels is sound physiology, yet there is no way to estimate his physiological age quantitatively; his development has to be measured against his time-age. Now the time-age of a plant is not a very useful measure, because a plant grows by localized meristems, and the branch of a tree, for example, may be ten years old at one end and ten minutes old at the other. Therefore any attempt

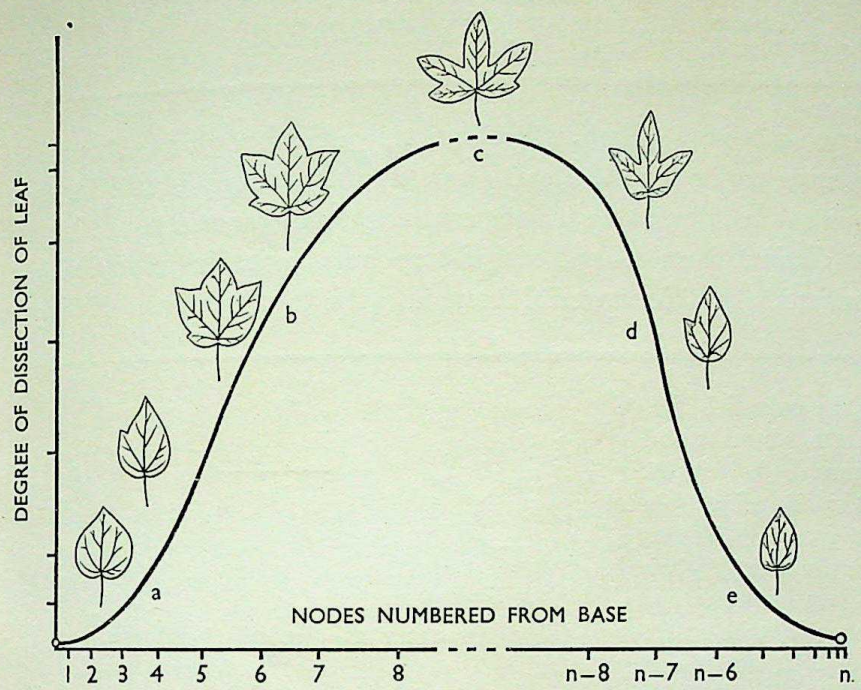


FIGURE 10 – *Diagram to illustrate the use of leaf shape in cotton to measure physiological age.* (*From a drawing by E. H. Roberts.*)

to measure the physiological age of meristems in plants, however tentative it may be, is worthy of serious attention. Krenke's work is such an attempt.

Using cotton, Krenke plotted the degree of dissection of the first, second, third, etc., leaves on a stem against the node number. He obtained curves of the general shape *abcde* (figure 10). He claimed that the shape of this curve represents the rate of ageing of the plant: the ordinates are the criteria of physiological age and the abscissae are units on a scale of development, as distinct from a time-scale. According to this hypothesis, external conditions which hasten flowering increase the slope of the curve *ab*, and the climax shape *c* is reached at a relatively early node; external conditions which delay flowering decrease the slope of the curve *ab*, and the climax shape *c* is reached at a relatively late node. Plants grown under different conditions may therefore bear leaves on corresponding nodes which have the same time-age but which are of different physiological age. This is exemplified by the sugar-beet leaves shown in figure 9 (from a paper by another Russian worker, Minina). Both leaves were on the sixteenth node and were about the same time-age. Leaf *a* is from an irrigated plant which will not mature early; leaf *b* is from an unirrigated plant which will mature early. On the criteria of leaf shape in sugar beet (see figure 8*c*) leaf *b* is physiologically older than leaf *a*. There is even some indication that the percentage of sugar in the root at any time may be roughly estimated from the shape of the last leaf which has unfolded.

A hypothesis as comprehensive as this cannot be accepted (however promising it appears to be) until something is known of its theoretical basis. There is at present no adequate theoretical basis for Krenke's hypothesis. His results indicate, however, that, among the problems of morphogenesis, the analysis of leaf shape is a problem of special significance. Nineteenth-century botanists have bequeathed us a rich legacy of observations on leaf forms in juvenile plants, amphibious plants, and so on. With twentieth-century techniques it will be possible to extend these observations considerably, and perhaps to extract from them an understanding of the causes and significance of leaf shape.

Some aspects of terpene chemistry

L. N. OWEN and J. L. SIMONSEN

For the organic chemist terpenes have a peculiar fascination, and although they have long received extensive and intensive study the chemical territory they occupy is still far from being fully mapped. The present article deals with some recent developments in the investigation of monoterpenes (as distinct from di- and sesqui-terpenes), including elucidation of the true nature of the odoriferous ketonic material irone and the total synthesis of pinene.

Terpenes are constituents of the essential oils of plants, and for many years there has been speculation on the possible mechanisms by which their biogenesis occurs. With a few exceptions, their chemical structures have been shown to be based on that of isoprene, C_5H_8; thus limonene, a typical monocyclic terpene, contains two isoprene units, while the sesquiterpene cadinene is built up from three such fragments (figure 1). It has recently

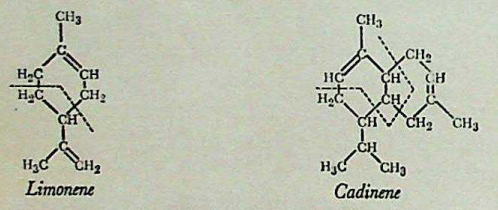


FIGURE 1 – *Isoprene structure of terpenes.*

been suggested [1] that isoprene might be formed in nature from the amino-acid leucine, derived by degradation of proteins, and it is tempting, therefore, to consider isoprene as a possible precursor of the terpenes, particularly since this hydrocarbon has been converted in the laboratory into a mixture of products containing geraniol, linalool, terpineol, sesquiterpene alcohols, and higher polymers [2]; it must be admitted, however, that somewhat vigorous conditions are necessary for these reactions to occur. An entirely different theory of the origin of terpenes [3] suggests that they are formed by condensation of saccharic and metasaccharonic acids, derived by degradation of carbohydrates; here also there is unfortunately little direct evidence to support the speculation. It is abundantly clear, however, that the biogenesis of a key compound, such as geraniol, would be sufficient to account for the formation of a large number of other terpenes, since interconversions can occur under comparatively mild conditions. A striking example is afforded by the recent laboratory synthesis of ascaridole (figure 2);

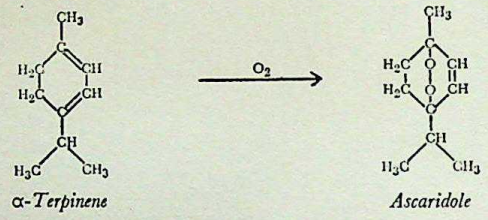


FIGURE 2 – *Synthesis of ascaridole.*

this has been obtained [4] by 1:4-addition of oxygen to α-terpinene, in the presence of chlorophyll and under the influence of ultra-violet light, a process which might evidently be responsible for the occurrence of this remarkable substance in nature. In view of the increasing availability of isotopic materials—particularly of radioactive carbon—it would appear that further advances in this interesting section of terpene chemistry may well result from the use of 'labelled' compounds in studies of plant metabolism.

Since the last decade of the nineteenth century, when many fundamental investigations on the structures of monoterpenes were being made, there has existed the *iso*propenyl—*iso*propylidene controversy over the position of a particular ethylenic linkage in the molecule [5]. It would be anticipated that a clear differentiation between the two structures under discussion, shown diagrammatically in figure 3, could be effected by oxidative degradation, particularly with ozone, when the

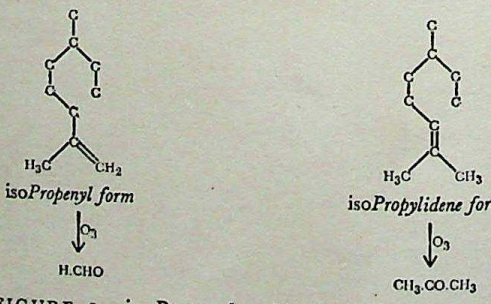


FIGURE 3 – iso*Propenyl and* iso*propylidene structures.*

*iso*propenyl form would give formaldehyde and the *iso*propylidene form would give acetone. Such chemical investigation of naturally occurring citronellal, geraniol, etc., has indicated that these terpenes are actually mixtures of the two isomeric modifications, different samples containing varying proportions, with the *iso*propylidene form usually predominating. Similar results have been obtained even on apparently homogeneous crystalline derivatives.

Physical evidence, on the other hand, is conflicting. In some instances it has been claimed that ultra-violet absorption spectra prove the existence of the *iso*propenyl structure only; in others the results indicate that the particular terpene consists only of the *iso*propylidene form. Measurements of Raman spectra have also been used to prove the homogeneity of, for example, geraniol, though for this particular substance the conclusion that it was the *iso*propylidene form was contrary to the evidence of the ultra-violet absorption spectrum; furthermore, instances are known where deductions from Raman spectra have been completely disproved by later chemical investigations. The interpretations of oxidative degradation have been criticized on the grounds that attack by ozone may not be limited to the ethylenic linkage, but though it is true that side reactions may occur to a small extent, it is highly improbable that they would do so in the degree necessary to account for the proportions of acetone and formaldehyde actually encountered. The most recent physical evidence—an investigation of the infra-red absorption spectra of various samples of citral, geraniol, and citronellol [6]—agrees with the chemical conclusions and indicates the existence of both the *iso*propylidene and *iso*propenyl modifications in the natural oils.

Although the majority of terpenes obey the 'isoprene rule,' there are a number of interesting exceptions (figure 4). Several are now known in which the isoprene units, instead of being arranged in the usual head-to-tail fashion, are joined irregularly; examples are found in lavandulol [7] and in artemisia ketone [8]. The C_{16} ketones angustione and dehydroangustione are built up from two isoprene units with one additional carbon atom [9]. The structure now assigned to leptospermone [10] represents a complete departure from the isoprene rule, and similar exceptions have recently been met in the sesquiterpene field, as shown by the constitutions adopted for eremophilone and its derivatives [11]. The discovery of such anomalies is important, since the structures

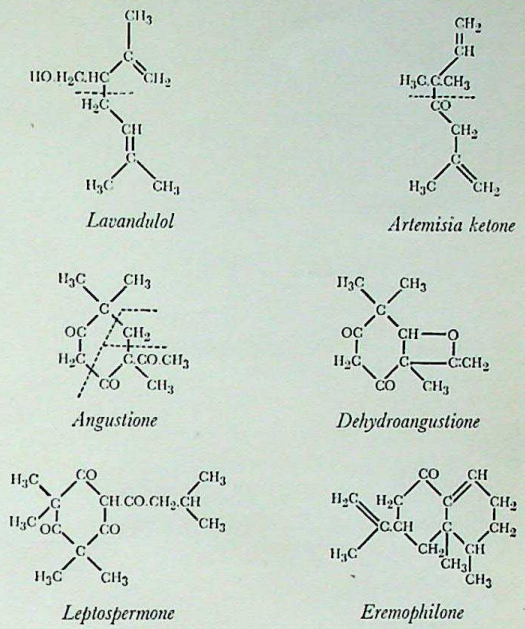


FIGURE 4 – *The isoprene rule: variations and exceptions.*

assigned to several sesquiterpenes have been based partly on the assumption of the validity of the isoprene rule, particularly in instances where the compound contains an 'angular' methyl group, such as, for example, in selinene. It is clearly desirable that the exact position of such angular methyl groups should be established experimentally, and this has been accomplished in the case of cyperone (figure 5) by direct synthesis [12],

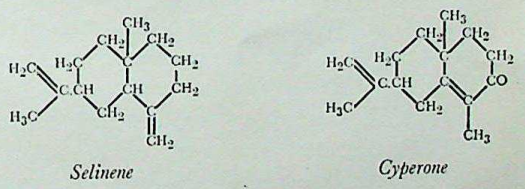


FIGURE 5 – *The angular methyl group in sesquiterpenes.*

thus confirming that the structure of this ketone does conform to the isoprene rule.

One of the most interesting recent developments in terpene chemistry has been concerned with the ketonic material irone, the odoriferous principle of orris root, the chemical study of which has now extended for over fifty years. Irone was originally thought to have the composition $C_{13}H_{20}O$, and although this was shown in 1933 to be incorrect [13] the error was perhaps a fortunate one, since it was largely responsible for the preparation and study of the ionones, the chemistry of which subsequently assumed such importance in connection with the structure of vitamin A and the carotenoids.

Irone is now known to be $C_{14}H_{22}O$, and in 1942 [14] it was formulated as a substituted cycloheptene (figure 6), since on ozonization followed by oxidation with chromic acid it gave ββγ-trimethylpimelic acid. It was realized, however, that

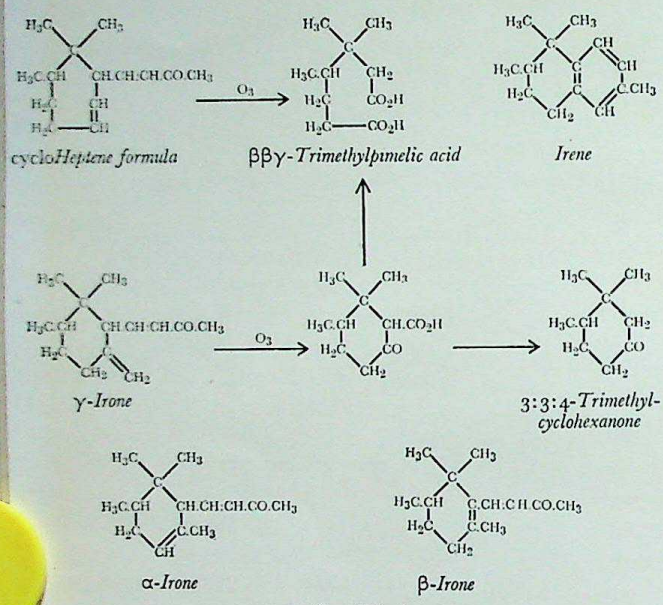


FIGURE 6 – *The irones.*

other ketones might be present in natural irone, for derivatives prepared by different workers frequently showed marked variation in properties; furthermore, it was difficult on the basis of the seven-membered ring structure to account for the conversion of irone into the tetrahydronaphthalene derivative, irene, the structure of which had been definitely established by synthesis. In a recent paper, however [15], describing further investigations on the ozonolysis of irone, it is established that formaldehyde and 3:3:4-trimethylcyclohexanone are products of this degradation, indicating the presence of a ketone with an exocyclic methylene group, now termed γ-irone (see figure 6). It is not unlikely that α-irone also is present, but it is not yet clear whether it occurs as such in the natural oil or is formed by isomerization of γ-irone during the isolation and purification process. The conversion of γ- into α-irone is readily brought about by treatment with weak acids, while with more concentrated acids, or with alkalis, β-irone is obtained.

The α- and γ-isomers possess the characteristic fresh odour of natural irone, the α- form being the more potent; the odour of β-irone, on the other hand, is similar to that of the ionones. α-Irone has now been independently synthesized by two groups of workers [16], an earlier synthesis [17] having given a product which consisted largely of the β-isomer. The formation of irene from either α-, β-, or γ-irone is readily understandable. The evidence for the existence of an irone having the seven-membered ring structure rests solely on the isolation of the trimethylpimelic acid from the oxidation products. Theoretically, it is conceivable that such an acid might be derived, by ring opening, from trimethylcyclohexanonecarboxylic acid, the primary product of the ozonization of γ-irone. If such a transformation could be shown to occur under the conditions employed, it would follow that there would no longer be any reason to postulate the existence of the cycloheptene form. It is significant that tetrahydroirone, obtained by hydrogenation of natural irone, is stated [15] not to be a cycloheptane derivative; it is probably 6-methyltetrahydroionone, but direct comparison with authentic synthetic material is complicated by stereoisomerism.

The problem of the total synthesis of pinene is one which has attracted the attention of organic chemists for many years. It has been attacked from two sides: the regeneration of pinene from its immediate degradation products, and the synthesis of these degradation products themselves. Although progress had been made in both directions, it is only recently that the gap has been closed. Broadly speaking, the investigations have followed two main routes, which are indicated in figure 7. The common starting-point is norpinic acid, a complete synthesis of which was achieved in 1929 [18]; eight years later [19] it was successfully converted into its higher homologue, pinic acid, from which in 1943 [20] pinonic acid was synthesized. The last step completed the synthesis of pinene by this particular route, since the conversion of pinonic acid into pinocamphone, and thence into pinene, had been accomplished [21] about twenty years earlier.

It should be mentioned that the difficulties inherent in these syntheses were intensified by the existence of stereoisomeric modifications of some of the compounds involved, so that the isolation of crystalline products was somewhat uncertain. It is unfortunate, for example, that the synthetic pinic acid could not be induced to crystallize, though it was identified by the formation of a crystalline anilide. From this point of view, the other route has proved to be more satisfactory.

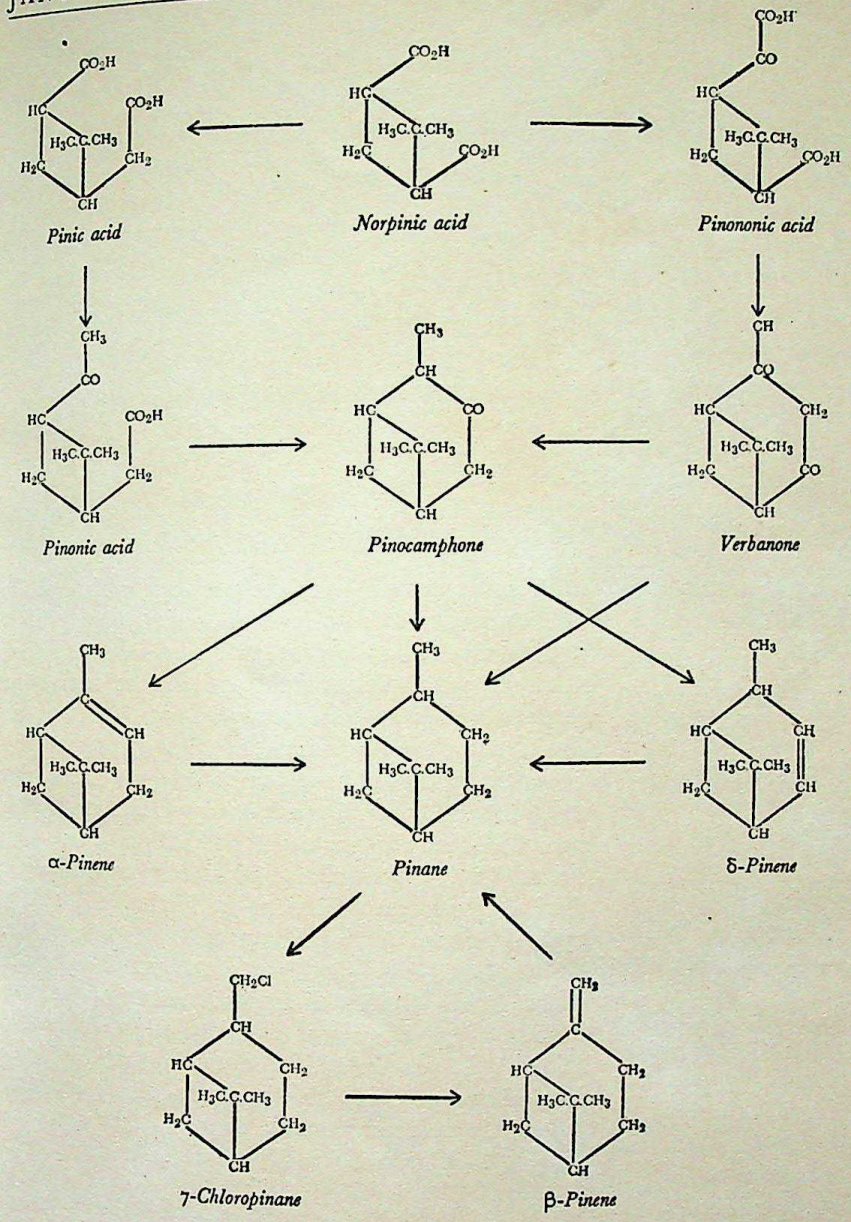


FIGURE 7 – *Synthesis of the pinenes.*

The first step, the synthesis of pinononic acid from norpinic acid, was reported in 1936 [22], and in the following year [23] the keto-acid was successfully converted into verbanone. The transformation of this ketone into the structural isomer, pinocamphone, was accomplished in 1941 [24] by the interesting sequence of reactions illustrated in figure 8, thus completing the last remaining stage in this series of syntheses. The saturated hydrocarbon, pinane, can be obtained by hydrogenation of any of the pinenes, and also by Wolff-Kishner reduction of verbanone or pinocamphone. On chlorination, one of the products is 7-chloropinane (figure 7), which on treatment with potassium phenoxide gives β-pinene (nopinene); this therefore constitutes a complete synthesis of the latter hydrocarbon.

An important synthesis of borneol and *epi*borneol was reported in 1939 [25]. Condensation of 1:5:5-trimethylcyclopenta-1:3-diene with vinyl acetate proceeded in both of the two possible directions; hydrogenation, followed by saponification of the products, gave *dl*-borneol and *dl-epi*borneol (figure 9).

During many reactions in the terpene field, particularly when bicyclic compounds are involved, molecular rearrangements are likely to take place. In earlier days, lack of appreciation of this fact resulted in considerable confusion in the literature and in much controversy between different groups of workers. It was eventually realized that transformations of the pinacolic type occurred under appropriate conditions, and when these led to a change of ring structure, they were classified as examples of the so-called Wagner-Meerwein change. A few examples were also known of pinacolic change without variation in ring structure, such as the formation of santene from camphenilol, but only comparatively recently has it become apparent that this simple isomerization is by no means an infrequent occurrence; it has been termed a camphene change of the second type, but is more usually referred to as the Nametkin change [26]. The appreciation of its existence has had several very important consequences, such as the re-formulation of a number of derivatives in the camphane series, but perhaps one of the most interesting is the explanation it offers of the facile racemization shown by camphene, bornyl chloride, etc., particularly under acid conditions. In the scheme illustrated in figure 10, *d*-camphene is shown to

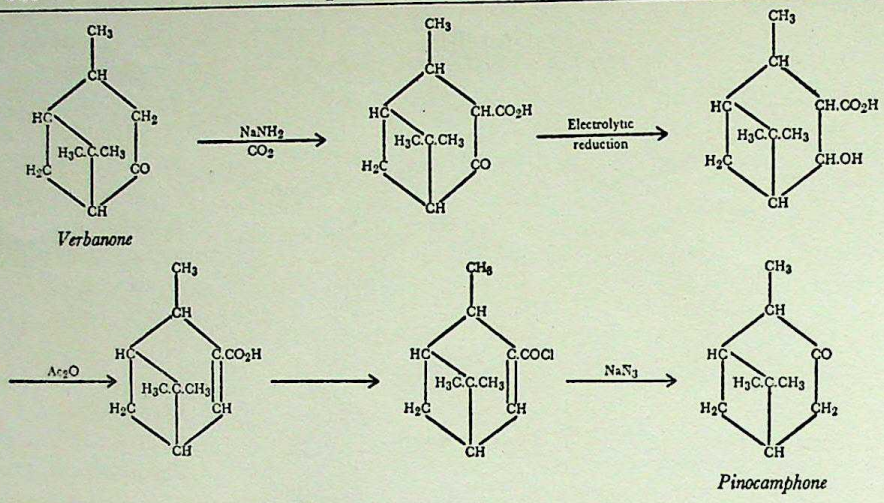


FIGURE 8 – *Conversion of verbanone into pinocamphone.*

give camphene hydrate on hydration; in this substance a pinacolic change of the Nametkin type, resulting in an interchange of the hydroxyl group

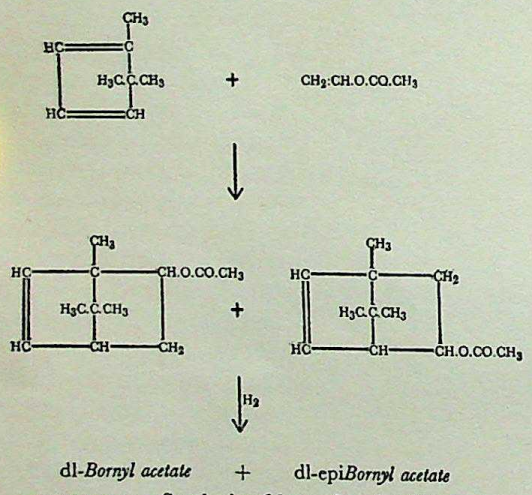


FIGURE 9 – *Synthesis of borneol and* epi*borneol*

with one methyl group on the adjacent carbon atom, results in the formation of a product which is still camphene hydrate, but of opposite stereochemical configuration, i.e. a derivative of *l*-camphene. Clearly, therefore, the camphene isolated from a reaction carried out under such conditions on either *d*- or *l*-camphene will be completely racemized. Similar considerations can be applied to the racemization of camphene in non-aqueous solutions.

In the example just quoted, complete racemization is the ultimate result of the Nametkin change, since the bridge heads are similar and the equilibrium proportions of the two hydrates must be identical. If, however, the bridge carries a substituent at one end, the product, although in the opposite stereochemical series, will differ structurally from its precursor and will therefore not be the enantiomorph. Furthermore, it may be formed in yield greater than 50 per cent., since the equilibrium proportions of the substances involved in the Nametkin change are no longer necessarily the same. By an ingenious application of this principle [27] it has been possible to carry out several interconversions of enantiomorphs (as distinct from racemization) in high yield, and a typical example is illustrated in figure 11. *l*-Camphor, $[\alpha]_D - 43°$, was converted into the α-dichloride, from which α-chlorocamphene was obtained by elimination of hydrogen chloride. When this was treated with trichloroacetic acid, it underwent both the Wagner-Meerwein and Nametkin rearrangements, to give, after saponification, 4-chloro*iso*borneol, which on reduction to

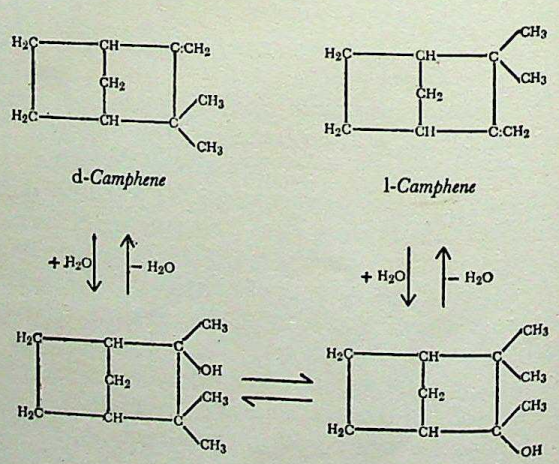


FIGURE 10 – *Racemization of camphene.*

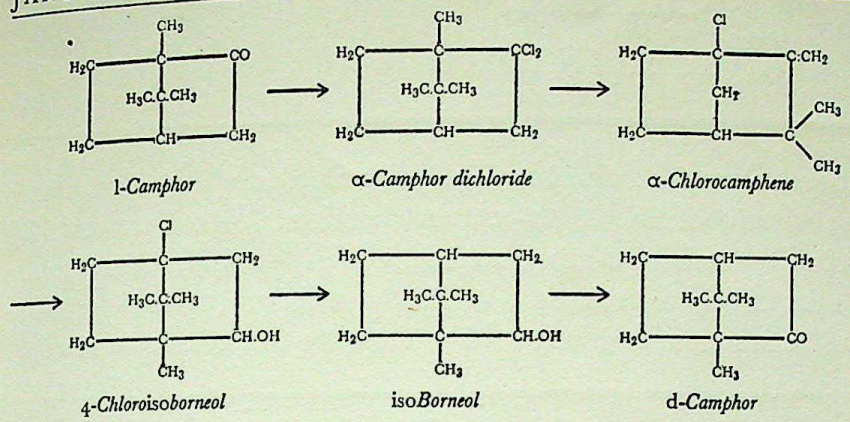


FIGURE 11 – *Conversion of* l- *into* d-*camphor.*

*iso*borneol followed by oxidation gave *d*-camphor, $[\alpha]_D + 32°$. This represents an 'optical conversion' of 74 per cent., the remainder having been racemized.

It has not been possible in this brief survey to refer to the many important developments which have occurred in the fields of sesqui- and di-terpene chemistry, though here, no less than in the realm of monoterpenes, many problems still await investigation. The unabated interest which is still shown in terpene chemistry will undoubtedly ensure continued advance in our knowledge of these fascinating substances.

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Curare

A. R. McINTYRE

Curare, one of the dreaded South American arrow poisons, is such a complex mixture that its analysis proved beyond the capacity of nineteenth-century chemists. It is, in fact, less than fifteen years since the first curare alkaloid, *d*-tubocurarine, was isolated and its structure determined. Biochemical studies of this and related alkaloids have led to important conclusions on motor-nerve and muscle function, and may lead to the conquest of muscle diseases.

The first account of South American arrow poisons was written by Peter Martyr D'Anghera and is found in the first 'Decade' of his *De Orbe Novo*, printed in 1516. These poisons were greatly feared, and with good reason. Inevitably, returning sailors told fantastic tales of the fearsome missiles showered upon them. Peter Martyr collected these stories, and many of them, often repeated by others, gradually became established and were deemed true. Thus it came to be believed that some venoms caused permanent 'hideous distortions of face and body, so horrible that no man could bear to look upon the victims'; others were alleged to produce insanity, 'they going endlessly about beating their heads on the walls' (Garcilasso de la Vega). Sir Walter Ralegh,[1] who is popularly but erroneously supposed to have first brought samples of arrow poisons to Europe, writing of them said, 'the partie shot indureth the most insufferable torment in the world, and abideth a most uglie and lamentable death, sometimes dying starke mad, sometimes their bowels breaking out of their bellies, and are presently discolored, as blacke as pitch . . . ' The ingredients were said to contain 'an underground tuber which flowers in the earth'; 'juices of trees, fangs of serpents, ants, stings of scorpions' (Gumilla), and the 'barke of the Roots of Couranapi, Baketi and Hatchybaly' (Bancroft), besides 'the fabulous coonycoochy snake' (Hillhouse).

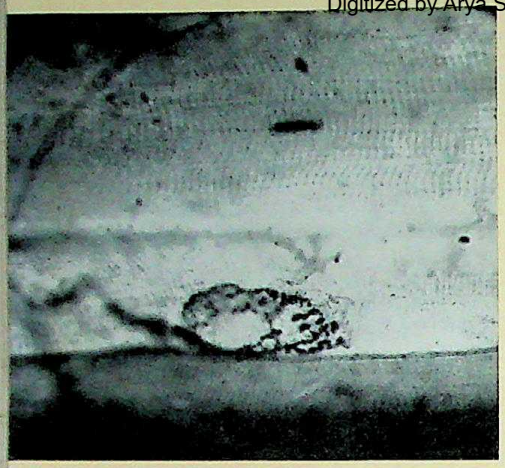
The poison of chief interest to scientists was curare. Curare is a generic name of dubious etymology, thought to be derived from the Indian word *urara* or its many variants, some of which are *urali*, *woorali*, and *woorara*. This is the poison the preparation of which was believed for centuries to be watched over by criminal old women of the tribes, 'who are made to take care of the boiling of the poison after shutting them up alone in a separate place so that, when the women die, 'tis a sign that the poison is sufficiently boiled . . . ' (De la Condamine). Curare to the physiologist designates a particular type of poison, which, upon gaining access to the blood, results in a loss of the normal motor-nerve control of the voluntary muscles. It is not surprising that the occurrence of a poison with so specific an effect aroused much interest, and from the eighteenth century until today botanists have sought to establish the identity of the plants used in its concoction. Humboldt was among the earliest to investigate the origin of curare; he believed the plants used were members of the genus *Strychnos* (*Loganiaceae*). Martius described five distinct types of poison, some of which contained specimens of *Cocculus* only. The Schomburgks saw curare prepared from plants identified as *Strychnos toxifera*. Present-day knowledge, briefly summarized, makes it certain that at least two main species, used either singly or together, are employed in the preparation of curare; these are several species of *Menispermaceae* (moonseed family) and *Strychnos*. The latter genus is widely distributed throughout the tropics, and the species *Strychnos nux vomica* of Asia is well known as the source of strychnine—an entirely different type of poison.

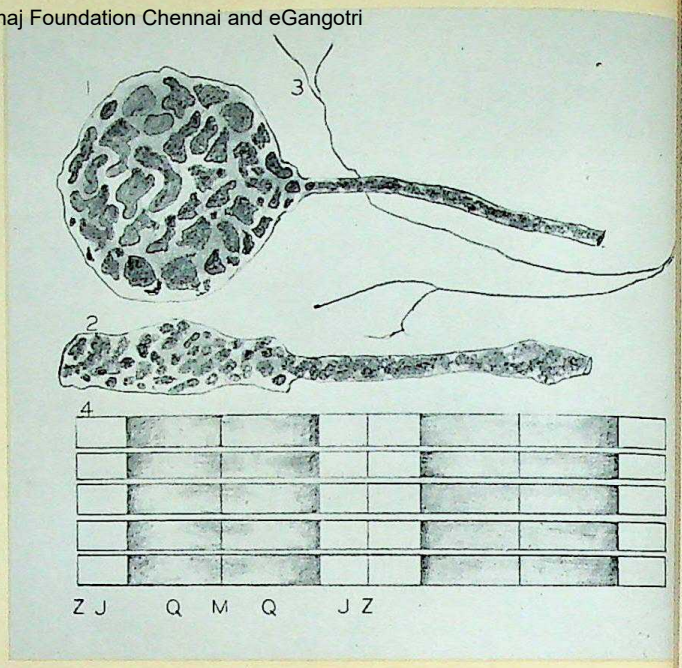
The botanist's task is formidable because, as is natural with primitive peoples, the Indians seek to surround the making of curare with mystery. They prepare it in the jungle at some distance from their villages and, contrary to legend, do not allow any female to come near the place of preparation. They mix many relatively inert ingredients with those that are active: some of these are certain plants and herbs (*Moraceae*, *Rutaceae*, etc.) said to be rich in gums and resins, which impart physical properties to the aqueous infusion such that it will adhere to the tips of the darts and arrows. The crude native product is a blackish-brown sticky mass with a characteristic odour, containing from 5 per cent. to sometimes as much as 17 per cent. of

[1] Sir Walter usually spelled his name without the 'i'.

FIGURE 1 – *Leaves of* Chondodendron tomentosum *and a piece of the rope-like vine.*

FIGURE 2 – *This illustration shows the native container (top, left) for the cotton which is placed on the blunt end of the dart j*





URE 3 – *Photomicrograph (above) of rat striated cle, showing motor nerves, end plates, and muscle ction. On the right are shown:*

Diagram of motor nerve end plate.

Same as 1, but turned through 90°. The end plate contains a lipid material which stains black with gold chloride.

Small motor nerves with no end plates.

Conventional diagram, showing the detail observable in the cross-striation of skeletal muscles. Muscle consists of elongated f a portion of five such fibrils is shown with their characteristic alternating dark and light bands. The darker bands seen under pol light are doubly refractive (anisotropic); the light bands are isotropic. Rollett designated the dark bands by Q, the light bands A fine membrane Z can be discerned in the light band. When the muscle is contracted the dark bands (Q) become wider. The of action of curare is at the junction between the nerve endings and the muscle fibrils.

Diagrams 1, 2, and 3 are drawn about $\frac{1}{16}$ the scale of diagram 4.

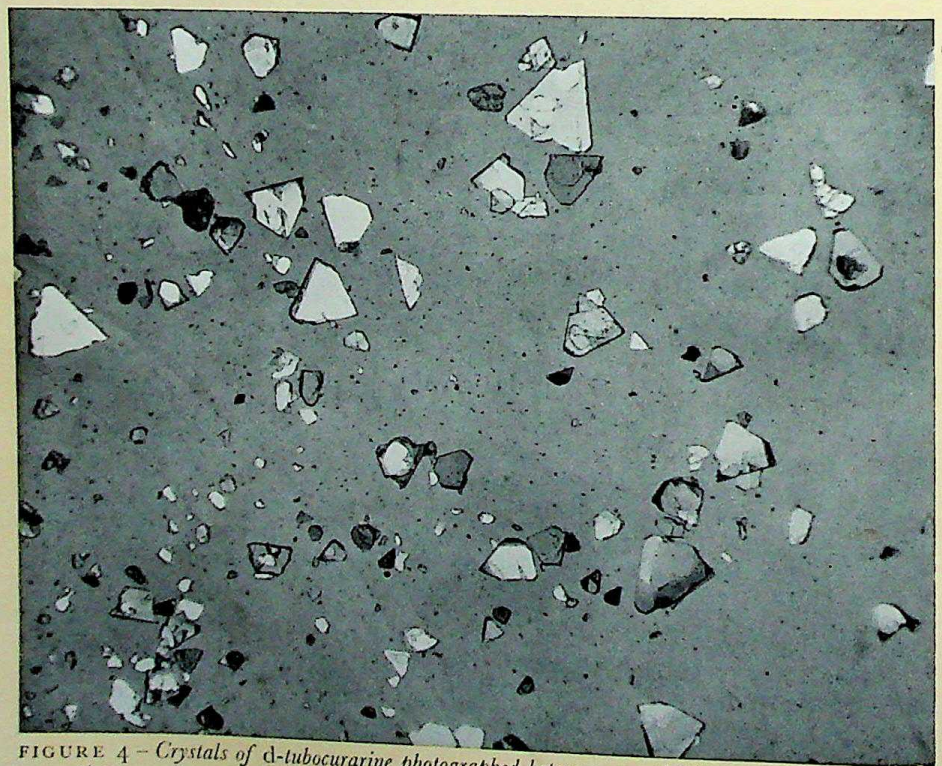


FIGURE 4 – *Crystals of* d-*tubocurarine photographed between crossed Nicol prisms, using a half-wave plate.*

alkaloids in the relatively inert mixture of saponins, carbon particles, and other extraneous matter. This mixture has frequently and with justice been described by the analytical chemist as 'difficult,' and the physical nature of curare largely accounts for the failure of early investigators, such as Boussingault (1827) and Pelletier and Caventou (1829), to isolate the pure alkaloids. In fact, it was not until the publication of King's work in 1935, on the isolation of *d*-tubocurarine from tube curare, that the chemical structure of the curares was established.

This was some forty years after Boehm had shown that curare contains two chief types of physiologically active alkaloids. The first, causing muscle paralysis, he named 'curarines'; they are quaternary bases. The second, which have direct effect on the blood-pressure, are tertiary bases; these he called 'curines.' It was Boehm who divided curares into three groups according to the container used by the natives—tube curare in bamboo tubes, calabash curare in gourds, and pot curare in earthenware pots. Today these distinctions are no longer reliable, and most of the large amount of crude curare that has arrived in my laboratory has come in old tins, sometimes with widely known trade marks still visible upon them. In America, Wintersteiner and Dutcher confirmed King's structure for *d*-tubocurarine and isolated it from a sample of *Chondodendron tomentosum*. It is a *bis*-benzoyl*iso*quinoline compound containing two phenolic groups. A number of closely related alkaloids have been obtained by King and also by Wintersteiner and Dutcher from other menispermaceous plants, e.g. *Ch. platyphyllum*, *Ch. microphyllum*, and *Ch. candicans*, and 'pareira brava.' The nature of the alkaloids in pot curare is still obscure, but they are possibly similar to the toxiferins and curarines obtained by Wieland and his associates from calabash curare. Wieland's work is noteworthy because he used an aluminium oxide adsorption column to isolate the alkaloidal Reineckate salts and the chromatographic method for their purification.[1] Of the alkaloids obtained, the toxiferins give a red colour with nitric acid, and the curarines a green and a violet colour with nitric and hydrochloric acids respectively.

Toxiferin I ($C_{20}H_{21}N_2,H_2O$, $[\alpha]_D^{20°} - 610°$) has extreme toxic potency: 0·3 grn is said to be sufficient to paralyse a frog. Two other curare alkaloids named strychnolethaline ($C_{22}H_{27}O_4N$) and curalethaline ($C_{25}H_{30}O_4N$) were isolated by Berrêdo-Carneiro from two samples of curare, and also from *Strychnos lethalis*. He found that they exhibited characteristic spectrographic absorption bands with peaks at 466 and 557 A for curalethaline and 559 A for strychnolethaline. With the exception of *d*-tubocurarine very meagre quantities of pure curare alkaloids are as yet available, and little beyond the fact of their high toxicity is known concerning them. Consequently nearly all the more precise physiological and pharmacological investigations with curare alkaloids have been made with *d*-tubocurarine or with curarines; the exact chemical nature of the latter is unknown. *d*-Tubocurarine is less potent than the toxiferins but produces a true curariform effect, i.e. it is capable of producing paralysis of skeletal muscle without significant direct effect upon the blood-pressure and respiration.

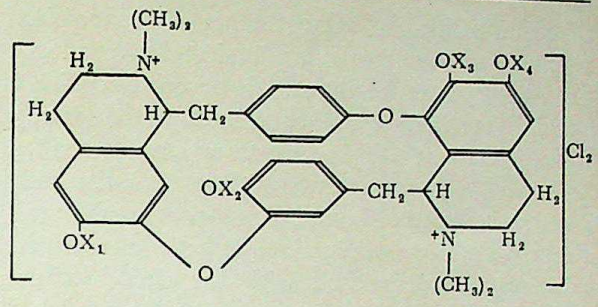


FIGURE 5 – *Structure of* d-*tubocurarine and related alkaloids.* (*Redrawn from Wintersteiner and Dutcher.*)

I. d-*Tubocurarine chloride:* $X_1 = CH_3$; $X_2 = H$; *of* X_3 *and* X_4, *one is H, the other* CH_3.

II. d-*Chondrocurine dimethochloride:* $X_1 = CH_3$; $X_2 = H$; *of* X_3 *and* X_4, *one is H and the other* CH_3, *but in an arrangement which is the reverse of that in I.*

III. d-*Tubocurarine dimethylether iodide:* $X_1 = X_2 = X_3 = X_4 = CH_3$; *anion* $2I^-$ *instead of* $2Cl^-$.

Ever since the classical experiments of Claude Bernard the precise mechanism of curare paralysis has been the subject of controversy, and, though the centennial of Bernard's work will soon be celebrated, no final agreement has yet been reached. The fundamental truth of Bernard's conclusions has never been seriously challenged. He showed that the poison does not affect conductivity in motor nerves or prevent the muscle from responding to a *direct* stimulus; the paralysis in a curarized animal is due to the inability of a motor-nerve impulse to stimulate the muscle. These observations very naturally focused attention upon the nature of the junction between motor nerves and muscles, and as a consequence the so-called motor end plates of nerves were discovered.

[1] For a description of the adsorption column technique, see a recent article in ENDEAVOUR by A. J. P. Martin (Vol. VI, 1947, p. 21).

These are disk-like enlargements of the terminal twigs of motor fibres, and their relatively large area appears to be in very close contact with a special portion of the contractile muscle tissue. Some, but not all, investigators have described changes in the appearance of these plate-like disks in curarized animals, and those who found alterations in the disks are inclined to believe that these changes are associated with the action of the poison. The changes can, however, be produced by many other substances; they are not specific to curare.

In addition to the discovery of the motor-nerve end plates, much physiological knowledge developed as a result of the investigation of toxic substances, and the study of curare has been directly or indirectly responsible for most of what we know concerning the nervous control of skeletal muscle. Thus the examination of the electrical irritability of nerve and muscle has resulted in the Lapicques' theory of chronaxie. This theory is based on the following considerations. When the negative pole of an electrical circuit is placed in contact with an excitable tissue and a current is applied, it will be found that the current, if made sufficiently small, fails to stimulate the tissue no matter how long it is applied. The smallest current capable of producing an effect is the 'rheobase' for that particular tissue. If now the rheobase current is doubled, the time necessary for the current to be applied in order to stimulate the tissue is relatively short; this period the Lapicques call *la chronaxie*; it is found to be constant for a given tissue. According to the Lapicques, nerves and the muscles they control have chronaxies approximately equal, i.e. they exhibit isochronism, but after poisoning with curare the muscle chronaxie is increased; hence the nerve and muscle exhibit heterochronism, and when heterochronicity is sufficiently marked the muscle will not respond to a nerve impulse. This theory of the Lapicques has been most fruitful in the promotion of carefully performed physiological experiments on the irritability of tissues in general, and notwithstanding the fact that the theory of isochronism has met with criticism and is by no means universally accepted, the Lapicques' work is of great importance, if for no other reason than that it provoked wide interest and very extensive studies of nerve and muscle electrophysiology.

The discovery by Langley that curare would prevent nicotine from producing contractions in both normal and denervated frog muscle was of much greater significance than was realized some forty years ago. His receptor theory paved the way for Loewi's investigations on the nature of vagus inhibition of the heart and the discovery that such inhibition was mediated by a chemical factor, namely acetylcholine. This compound makes its appearance as a consequence of vagus nerve activity. Subsequently the role of acetylcholine in nerve-muscle transmission was examined by Dale and others, who found that when motor nerves to skeletal muscles are stimulated acetylchloine can be detected in the fluid perfusing the muscle. It soon became apparent that curarization could be explained by assuming that curare interfered with the effect of acetylcholine on the muscle. Recently Kuffler and Gerard have shown that some of the skeletal muscles of frogs are controlled by two distinct types of motor nerves; the larger nerve fibres appear to be responsible for quick movements of the muscles and the smaller fibres cause steady muscle contraction or 'tone.' Significantly, the smaller nerves do not appear to terminate in end plates. It is known that mammals, including man, also possess at least two types of motor nerves. Curare prevents muscle excitation by the small fibres more readily than it interrupts excitation by the larger nerve fibres. Thus, the muscles supporting the head in an animal such as a rabbit are normally in a steady state of tonus, and these muscles are rather quickly paralysed by curare. On the other hand, during life the muscles of the diaphragm are in almost constant motion, and these are not, at first, noticeably affected by curare. Advantage is taken of these facts in the use of the rabbit as a test animal for the bio-assay of curare preparations. The test is known as the rabbit head-drop test, and was first used by Holiday.

After the use of curare by Sewell for the treatment of tetanus in horses, in England, curare was first used in human tetanus by Sayres, in New York, in 1858. Although curare has been used from time to time in man for a variety of conditions ever since, it is only quite recently that sterile standardized preparations have been readily available, and the modern use of curare in the clinics began with the work of West in England, Griffith in Canada, and Burman, Denhoff, and Bennett in America. Today curare is used very widely and is found particularly useful as a means of increasing muscle-relaxation during anaesthesia. For example, a patient lightly anaesthetized with cyclopropane may be given an intravenous injection of a standardized curare preparation, when the abdominal musculature will promptly relax, rendering the viscera accessible.

Deep anaesthesia is thus avoided, thereby adding considerably to the safety of the patient. Ether has been shown to possess a curare-like action, so when curare is used in ether anaesthesia the dose of curare must be reduced to less than half that used with cyclopropane. The use of curare in dislocations also greatly facilitates the surgeon's task. In such cases there is nearly always strong reflex spasm of the muscles, which necessitates the application of considerable force to relocate the articulating surfaces of the joints involved. The use of curare renders such manipulations relatively easy, and as the muscle spasm is abolished the pain is markedly reduced.

The use of electric shock therapy for the treatment of certain types of psychotic patients is sometimes complicated by injuries suffered during the electrically produced convulsions. Today in many psychiatric hospitals curare is used as a matter of routine to prevent muscle, tendon, ligament, and bone injuries formerly encountered. The use of curare in the treatment of chronic spastic states was carefully examined some years ago by West. The recent fundamental physiological work of Kuffler and Gerard indicates that the use of curare in such conditions has a theoretically sound basis, and this work may lead to an explanation of the early discoveries of Bremer, who described a decrease in the hypertonicity of muscles in decerebrate animals when injected with curare. Similarly the effect of curare in parathyroid tetany, described by Hartridge and West, is rendered more understandable. The effects of intravenous injections of aqueous solutions of curare are somewhat transitory; hence, in the treatment of chronic spasticities, oil and wax suspensions of the alkaloid *d*-tubocurarine have been utilized which, when injected intramuscularly, are absorbed sufficiently slowly to enable a moderate degree of curarization to be maintained for as long as seventy-two hours. Such preparations containing *d*-tubocurarine, or possibly, in the future, other related alkaloids, may prove of value in chronic spastic diseases.

Contrary to general belief, the clinical use of *d*-tubocurarine, or preparations such as Intocostrin, which was first prepared in the author's laboratory and which contains *d*-tubocurarine, is not attended with much risk, because, should the safe dose be accidentally exceeded, artificial respiration and the prompt injection of the antidote neostigmine will at once overcome the paralysis. Hence it is customary to have neostigmine at hand when curare is used. However, some types of curare preparations, particularly those containing certain toxiferins or curarines, are likely to be dangerous because of their effect on smooth muscle, particularly the bronchial musculature. Much interest has been aroused by the discovery that the muscle disease *Myasthenia gravis* renders a patient very sensitive to curare; such patients can tolerate only a fraction of the normal dose. It is of considerable significance that neostigmine, the most effective drug in this disease, is also by far the best antidote for curare poisoning. Hence some investigators suspect that the disease *Myasthenia gravis* may be caused by a substance having a curariform effect. The source of this substance is unknown.

Figures 1, 2, and 4 by courtesy of Dr H. S. Newcomer of E. R. Squibb and Company, New York. Figure 3 by courtesy of the Department of Anatomy, University of Nebraska College of Medicine, Omaha, Nebraska.

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Some aspects of modern laboratory design

J. YULE BOGUE

The design of a new laboratory is of great importance, for under modern conditions of highly specialized work the building must be looked upon not merely as providing accommodation for the research workers but as an integral part of their permanent equipment. Apart from the usual services, special facilities may be needed. Thus biologists and medical workers may require animals for experimental work; research on viruses and infectious diseases may require elaborate arrangements to prevent infection of staff and experimental animals.

The modern research laboratory, besides housing the research worker and his apparatus, should be considered as forming part of his equipment. It is unfortunate that this most essential part of his research facilities has not, until the last ten or fifteen years, received as much specialized attention and investigation as has been devoted to other aspects of his work. Perry Coke Smith (1947) points out that the organization of laboratory space and its mechanical services into a smoothly functioning and easily maintained whole has generally been provided for the research worker by independent authority, rather than in response to his demands.

Although it is not possible to lay down a universal specification for a research laboratory, a study of the more recently constructed academic, government, and industrial laboratories reveals a remarkable similarity in the basic requirements, in spite of a wide range of specialized activities. This is borne out by the general acceptance of the repetitive space pattern or module system. The module may be defined as the minimum space within which a single worker can carry out his research, and which therefore contains within itself all service outlets and points, illumination, ventilation, and other direct services which are brought to the work area.

While the dimensions of the module may vary in different laboratories, there is fairly close agreement on the amount of space which should be allocated to each qualified worker. The average figure appears to be around 280 square feet per man. This area includes the floor area (free and covered) available to the research worker. It excludes corridors, stairways, toilets, library, store and workshop facilities, and all other indirect services which are not available at the bench.

A gross area of the order of 500 square feet per qualified man would seem to cover most research activities other than those requiring pilot plant facilities and other specialized equipment of large size. In assessing the gross area for a biologist, animal houses, isolation areas, and sterilizing facilities have to be considered. These and other requirements may involve an increase in gross area up to 2,500 square feet or more per qualified man, depending upon the type of work. Biological facilities of this type are considered below.

The module ensures that this minimal space may be used as a one-man laboratory, while any multiple of the module-width can be utilized for laboratories of different sizes, thus making for maximum flexibility. The one-man module is not often used; a two-man module laboratory appears to be the more usual minimum, particularly in industrial laboratories.

The module partitions are non-structural and are usually made of hollow tile with plaster finish, of terra-cotta tile with semi-glaze finish, or, as in the case of the Bell Telephone Laboratories, New Jersey, of movable steel partitions constructed in sections. The steel panels are of double-sheathed construction packed with sound-absorbent material. These panels can be erected at any multiple of six feet. In Britain, plastic partitions (Holoplast) are being tried. Steel or plastic partitions have the advantage of extreme flexibility, since it is possible to remove and re-erect them with the minimum of interference and with the aid of only a hammer and screwdriver. The removal of tile or plaster partitions, though practicable, results in much dust and disturbance during the process.

There is a considerable difference of opinion with regard to the provision of office facilities for the worker at the bench. From his viewpoint the ideal location is immediately adjacent to, but separated from, the actual work area. The only way in which this can be achieved, with preservation of maximum flexibility, is to partition space primarily designed and serviced for laboratory

purposes. This enables the office to be located anywhere in the laboratory wing and relocated at any time. A more economic use can be made of the space if, for example, the part on the window side is allocated to office purposes, while that on the corridor side is used for others.

Such a layout is shown in figure 1, which is of the standard laboratory unit adopted by the U.S. Department of Agriculture at their Western Regional Research Laboratory. This laboratory module is 16 feet wide by 24 feet deep, with a floor-to-ceiling height of 10 feet 4 inches. The unit is made up of three such modules, namely two laboratories, each of one module, separated and served by a central module divided into two 8 by 13 foot studies on the window side and an 11 by 16 foot utility room on the corridor side. The partitions within the central module are of portable steel units. The utility room can be used for a variety of purposes, such as constant-temperature room, microscopy room, Kjeldahl area, and so on. On the basis of two qualified men per laboratory, this unit provides a working area of 288 square feet per man.

Such a type of laboratory suite can, of course, be extended to serve several laboratories. In this case the junior workers would have their desks in the laboratory. The number of qualified people occupying the office should not exceed two; single occupancy is preferred. The laboratory office should, if possible, have a transparent panel through which the occupant can observe the activities in his laboratory. Where such individual or two-man offices cannot be provided, the worker at the bench should have in his laboratory a desk, a filing cabinet, and some enclosed bookshelves. This is more desirable than an office in a short wing, or at the end of a laboratory wing relatively remote from the work area.

The laboratory office, of whatever type, is not necessarily the area in which the research worker will do his hard thinking. Such work requires close contact with the literature, so that the above facilities must be supplemented by the provision of study rooms in the library area. While engaged in this type of work the research worker should be given sole occupancy for several days, or, if necessary, even for a few weeks.

The generally accepted services include hot and cold water, steam, gas, air, vacuum, and electricity, both single and three-phase. Most laboratories now provide distilled water in block tin or aluminium pipes to single points in each laboratory, or to selected central points in corridors, by gravity feed from a pair of central stills. The risk of contamination, however, may deter the provision of this service. In the interests of reliability it is necessary to carry out regular conductivity tests every few days. As distilled water is an expensive service, the outlet valves should be spring-loaded.

Since the highest possible density of outlets in the laboratory is desired by the research worker, they should be in groups at close intervals. A considerable economy in respect of the main service capacity and loading can be effected by previous study of the number of outlets in use at any one time in a number of different laboratories. The actual number in use at any one time may be considerably less than 10 per cent. of those provided.

It is undesirable to trundle gas cylinders into laboratories. The cylinders should either be housed and connected to local laboratory lines in specially designed cylinder cupboards within the corridor service walls, with access from the corridor only, or be kept on such balconies as have been provided for escape and shade purposes. In this case access to the balcony should be from landings and not through the laboratories. In large laboratories, nitrogen may be supplied from nitrogen cylinder trailers connected to manifolds outside the building.

Except in physical, electrical, and other special laboratories, low voltage (from two volts upwards) and D.C. are not universal. Some workers state that while the D.C. and low voltage are a convenience, it is an expensive one; single- and three-phase supply are, however, essential.

The service piping, conduits, and lines, whether they be vertical or horizontal, on external walls or within corridor walls, need no longer be exposed to ensure accessibility; removable panels or proper doors in corridor walls give adequate access. The essential feature of the service layout is that any of the services may be modified or changed without interrupting the services of adjacent modules. The piping, conduits, and outlets at the bench should be removable. They may be hung on the walls above or below bench height, or on racks which are readily removed. This latter method is used at the Shell Development Company's laboratories, Emeryville, California.

The lighting intensity in different laboratories varies from about 15 to 38 foot-candles. The research worker prefers an intensity of some 30 foot-candles. Lighting by fluorescent tubes in

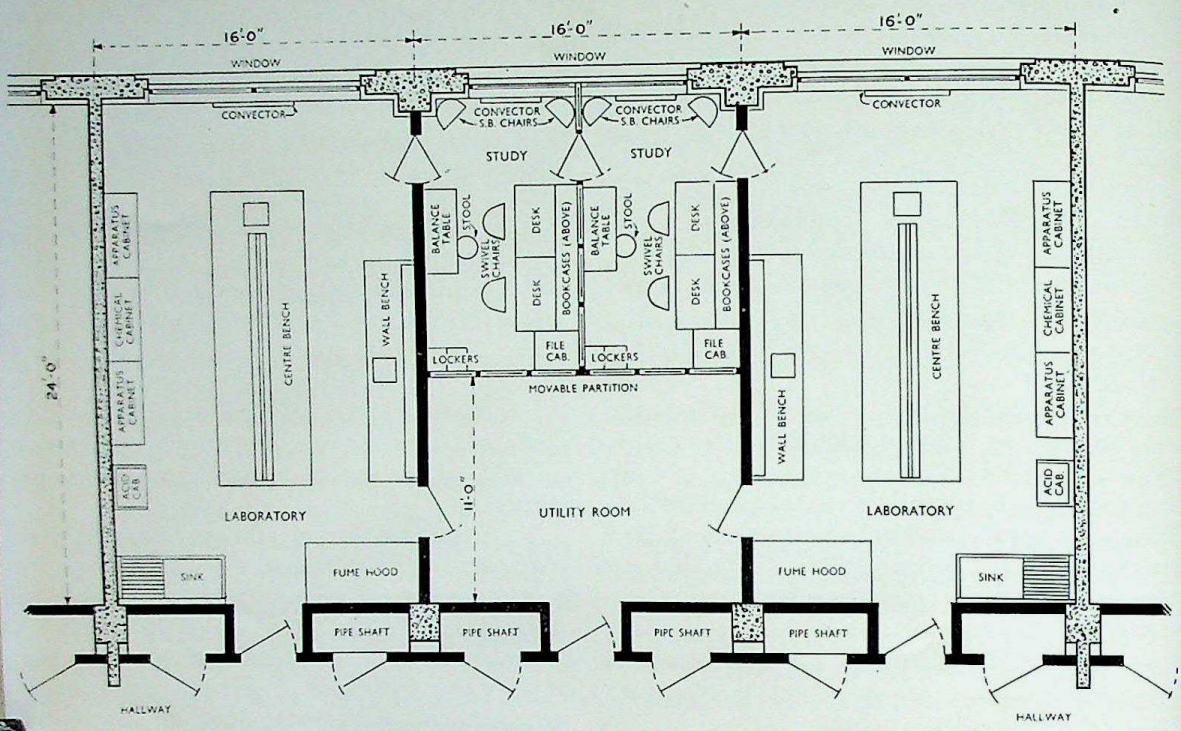

FIGURE 1 – *Standard laboratory unit, Western Regional Research Laboratory, U.S.A.*

recessed fittings is most favoured. It is considered desirable to fit diffusers, preferably of plastic as a protection against accident.

Where fume hoods are necessary, they should have individual fans controlled from the hood of origin. It is an advantage to have one half of the work table removable by the chemist to permit the ventilation of taller equipment. The provision of a ventilated area as well as a proper fume hood is also useful.

All are agreed on the advantages of a completely air-conditioned laboratory. This is expensive, however, as recirculation is out of the question and the fume hoods carry a large volume of treated air away. Beach (1947) believes that this latter problem has been solved by a new 'pressurized' or induced draught hood as fitted in the recently completed B. F. Goodrich laboratories. Air-conditioning is essential for micro-analytical and other special-purpose laboratories. Forced ventilation with filtered and washed air should be provided where air-conditioning is not installed. As constant-temperature rooms are necessary in biological laboratories there should never be less than one hot and one cold room per floor. It has been suggested that an equivalent area of one module in every twelve should be set aside for this purpose.

The module system logically demands an assembly of movable standardized sectional units such as table, cupboard, and drawer. These are usually made of steel, which is protected by lead-flashing the copper-loaded metal, or by some other rust-preventing process, and finishing them with baked enamel. The Mellon Institute uses a demountable metal framework, the components of which are fitted firmly together without the use of bolts or screws. The only tool required for erection or demounting is a rubber mallet. The framework supports the bench tops and sinks, and accommodates the cabinets and drawer units. Bench tops may be of wood, soapstone, plastics, or stainless steel. The recent developments in plastics have opened up a wide range of properties, finishes, and colours.

There is as yet no ideal floor covering; those most commonly used are battleship linoleum, asphalt tile, rubber, and cork, all of which are readily repaired. Quarry tile and concrete are not favoured by those standing at the bench.

While the biologist and medical research worker can carry out most of their activities in suitably arranged modules, they require additional and specialized facilities for their experimental animals. Even in a single institute these facilities may require the provision of properly

designed and serviced areas to house insects, aquaria, mice, rats, rabbits, guinea-pigs, cats, dogs, and monkeys. In some cases there may be many of the larger domesticated animals. These requirements add considerably to the gross space allocation per man. Omitting the larger domesticated animals, the ratio of gross animal house area to laboratory area seems to vary between 1·7 : 1 and 0·7 : 1.

Apart from the problem of special isolation quarters for virus and highly infectious diseases, opinion is approximately equally divided on the desirability of housing the animals in the laboratory building as opposed to an entirely separate building. Where animals are kept in the laboratory block, the majority of workers are in favour of segregation, either by devoting a strategically placed floor to animals or by double air-lock isolation on several floors. It is not considered desirable to mix animal rooms and laboratories. Where the animal need not be brought into the laboratory, the ideal solution appears to be a separate animal block provided with special manipulation and operation areas. In addition to the animal quarters proper, the facilities must include reception, quarantine, and treatment areas for imported stock, sterilizing equipment for bedding, food, cages, and utensils, incineration for bedding and animals, diet-mixing areas, kitchens, and cold stores.

There appears to be a general agreement that air-conditioning with local temperature control and boost heaters is the ideal method of achieving standard environmental conditions. There must be no partial recirculation of air. Laboratories which are not air-conditioned usually provide local equipment for the rat and mouse breeding units. The animal room surfaces must be capable of withstanding hot washdowns at intervals.

While it is not possible within the scope of this article to discuss the details of animal houses and biological laboratories, the special facilities required for investigations into virus and highly infectious diseases should be mentioned. The National Institute of Health's Virus and Infectious Diseases Laboratory at Bethesda is an example of a highly specialized occupancy problem. Every precaution has been introduced to prevent infection of workers and cross-infection of animals. The building consists of three laboratory floors proper, each of which consists of two identical laboratory wings served by a central 'clean' area. The working of the unit is dependent upon a complex air-conditioning equipment, which maintains the air pressure at a higher level in the central clean area than in the laboratory wing, where in turn the corridor air pressure is higher than that of the animal rooms and laboratories. Air supplied to certain areas, such as the sterile cubicles, is irradiated with ultra-violet light and

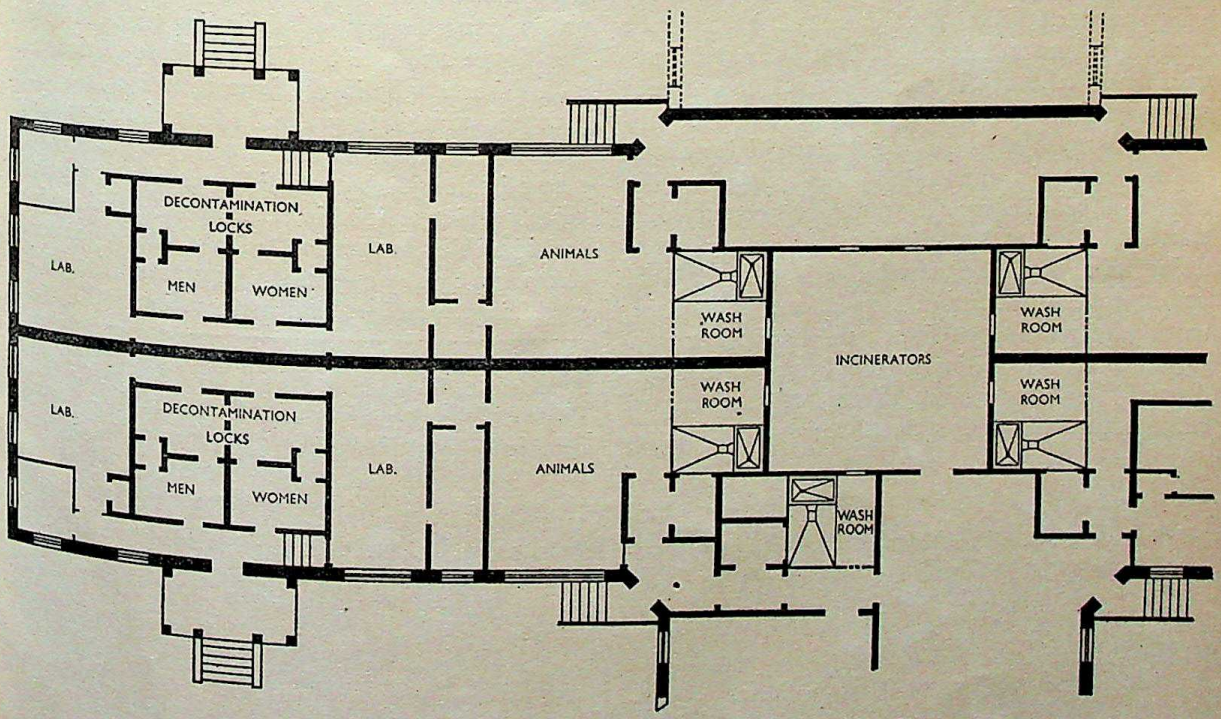

FIGURE 2 – *Preliminary layout of Merck isolation building, New Jersey.*

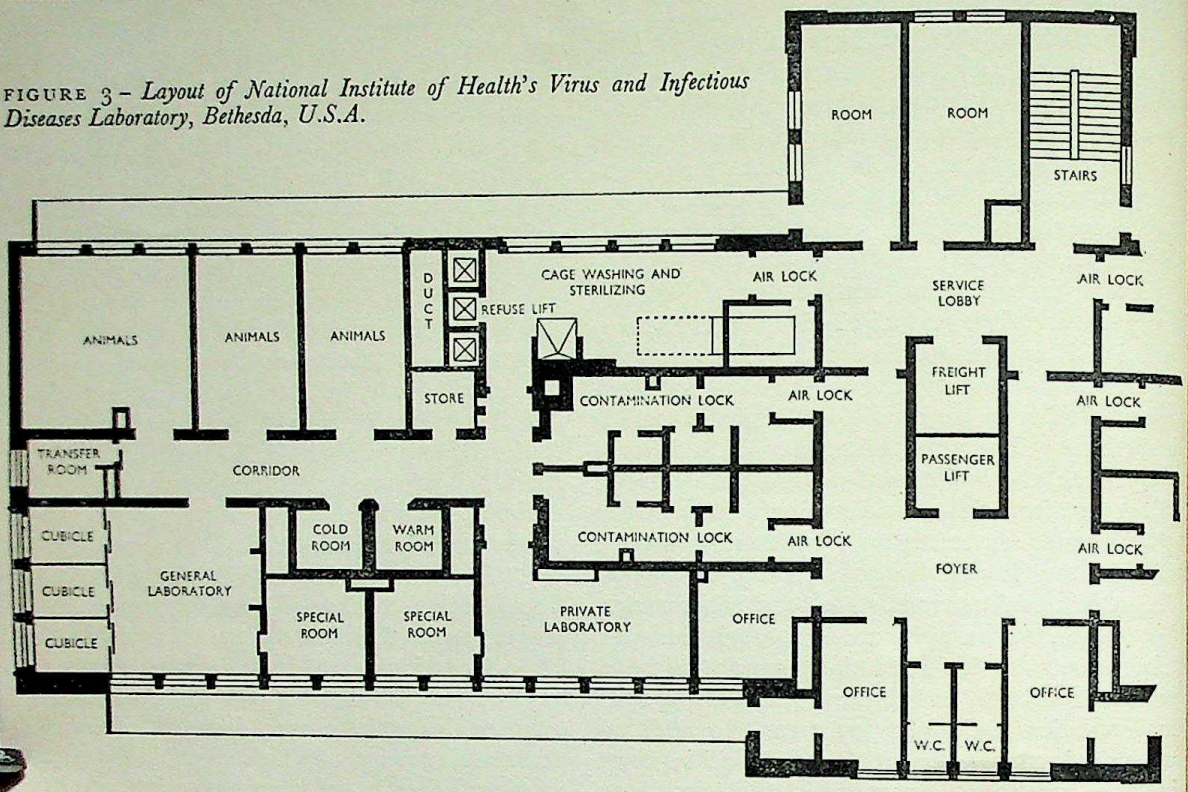

FIGURE 3 – *Layout of National Institute of Health's Virus and Infectious Diseases Laboratory, Bethesda, U.S.A.*

passed through spun glass filters. The exhaust air from these areas and hoods is sterilized by passing it through electric grills. Figure 3 shows the layout of one of the two identical laboratory wings on each floor. The essential features are dressing rooms and decontamination locks, small and large laboratories with special rooms and sterile cubicles, constant-temperature rooms, animal rooms, and cage washing and sterilizing room.

In these units rather less than half the floor area is available for laboratory space; about a third is taken up by animal quarters and sterilizing area, and the remainder is taken by the contamination locks and circulation. All writing work, the reading of literature, and other non-experimental activities of the workers, are conducted in offices and rooms of the central clean areas. No desk space for non-experimental work is provided within the laboratory units.

Merck, at Rahway, New Jersey, have suggested another approach to the prevention of infection, the general principle of which is shown in the preliminary layout of their isolation building (see figure 2). The building is single-storied and will ultimately be in the form of a cross, with the root accommodating the incineration, washing, and sterilizing facilities. Each wing is divided along its length by a solid wall into two completely self-contained infected areas. Here again a considerable proportion of the floor space is taken up by the essential decontamination locks, sterilizing, washing, and incineration facilities.

The author gratefully acknowledges his indebtedness to American colleagues and Institutions for placing many of the essential data at his disposal, and for their generous assistance and co-operation.

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Blood-pigments

H. MUNRO FOX

In vertebrate animals haemoglobin is the respiratory blood-pigment which transports oxygen from lungs or gills to muscles and other tissues. Among the invertebrates, some have haemoglobin but others have a related green pigment, chlorocruorin, or the blue haemocyanin, while yet others have no blood-pigment at all. Substances nearly related to haemoglobin and chlorocruorin are found in tissue cells of all animals. The functions, relationships, origin, and evolution of the respiratory pigments are discussed in this article.

Blood is coloured because it contains a respiratory protein. This means a chemical substance which can attach dissolved oxygen to itself and then give it up again when the pressure of oxygen in the surroundings is low. Haemoglobin is such a substance. It enables our blood to carry forty times the amount of oxygen from lungs to muscles, brain, and glands that water could transport in solution. As we need this oxygen, we could not exist without haemoglobin, for clearly it would be impossible to have forty times our normal volume of blood. All vertebrate animals possess haemoglobin. Many invertebrates also have blood which is red with haemoglobin. Some, however, have a similar green pigment, others have blue blood, while yet others have no pigment at all in their blood. The octopus and the snail have blue blood. So have lobsters and crabs. This colour is due to haemocyanin [1], which is another respiratory protein, with copper in its molecule and not iron as in haemoglobin. Figure 7 (*a*) shows blue oxyhaemocyanin; deoxygenated it is colourless. Figure 7 (*c*) shows scarlet oxyhaemoglobin and figure 7 (*b*) the purple deoxygenated pigment.

Haemoglobin has a greater affinity for carbon monoxide than for oxygen. For this reason carbon monoxide is a poison, though some animals are not quickly killed by it. For example, the so-called blood-worm, the red larva of a midge, *Chironomus*, which lives in its millions in mud on the bottom of lakes, has haemoglobin in its blood. As long as the lake water is well aerated, the insect's haemoglobin is not used. The oxygen in simple solution in the insect's blood is then enough for its wants, and so one cannot at once kill the larva with carbon monoxide. However, in the mud where the insect lives oxygen is often scarce, and it is then that the haemoglobin comes into action (R. F. Ewer). It picks up the little oxygen available in the muddy water. The insect can indeed live for quite a long time with no oxygen at all, but such anaerobic life is costly, using up much stored food, and the insect keeps quite still when in the anaerobic state, not even feeding. Haemoglobin enables it to use the last traces of oxygen in the pond, staving off the anaerobic state (Walshe [2]).

Another invertebrate animal with haemoglobin in its blood is *Daphnia* [3]. This is a small crustacean abundant in many ponds, which Schwammerdam, in the seventeenth century, called the Arborescent Water-flea (figure 2). The haemoglobin in the blood of *Daphnia* has apparently no respiratory function. By means of carbon monoxide one can render the pigment incapable of carrying oxygen. With its haemoglobin thus inactivated, the animal goes on swimming for hours as vigorously as before, no matter how low the dissolved oxygen content of the water may fall. But *Daphnia* has an unexpected use for its blood-pigment. Female *Daphnia* carry their eggs in a brood-pouch (figure 4). Here the eggs develop in a couple of days into young, which then swim away. In the brood-pouch the eggs risk partial suffocation, since there is no free communication with the outside water. The eggs of *Daphnia* differ from all others in that they contain haemoglobin: see figure 4. Experiments have shown that the eggs develop less rapidly when their haemoglobin is put out of action by carbon monoxide. Thus the haemoglobin in the eggs does possess a function. Now, most surprisingly, during the few hours before the eggs are laid in the brood-pouch, while they are still in the mother's ovary, they become visibly pinker, while at the same time the blood of the mother becomes measurably paler (E. I. B. Dresel). The blood of the *Daphnia* supplies the eggs with haemoglobin. Here is an unexpected function for the blood-pigment.

In the study of haemoglobin, *Daphnia* is also remarkably interesting for a different reason. This is that the quantity of haemoglobin present in its blood varies very greatly. *Daphnia* in one

pond may all be pale; the same species in another pond can be so red that the whole water seems coloured. As Schwammerdam wrote, 'the water appeared as if changed into blood, which, indeed, terrified me at first.' One and the same individual *Daphnia* can change in the course of a few days from being almost colourless to red, and *vice versa*. The contrast is well seen in figures 2 and 3. The cause of an increase in haemoglobin in the blood of *Daphnia* is a low oxygen content of the water in which the animal lives. It was once thought that the increase in blood-pigment of *Daphnia* was due to their eating green algae. This was explained by the chemical similarity between chlorophyll and haem, the coloured part of the haemoglobin molecule, for both chlorophyll and haem are built up from porphyrins, cyclic compounds with four pyrrol rings. In fact, however, chlorophyll in the food does not produce haemoglobin in *Daphnia* (S. M. Hardcastle), any more than patent medicines based on chlorophyll cure human anaemia. In point of fact, *Daphnia* in a polluted farm pond lacking oxygen behave like human mountain climbers, for extra haemoglobin appears in a mountaineer's blood in response to an oxygen deficit in the air.

In mammals, red blood-cells with haemoglobin are formed in the marrow of bones. This is an unexpectedly out-of-the-way place for such an important synthesis. Could the cause of it be that there is perhaps in the bone marrow a backwater of the blood-stream in which oxygen is deficient? The events in *Daphnia* and in mountaineers suggest that haemoglobin may be a by-product of semi-anaerobic metabolism. Once, in early geological times, some hundreds of millions of years ago, haemoglobin must have been synthesized in an animal for the first time. To begin with, it may well have been merely a useless by-product of semi-anaerobic life. Later on, the usefulness, in some cases, of haemoglobin as an oxygen carrier or an oxygen store would have assured its preservation through natural selection. In other cases it may still occur as a useless by-product, in yet others as a vestigial remnant of a substance formerly useful.

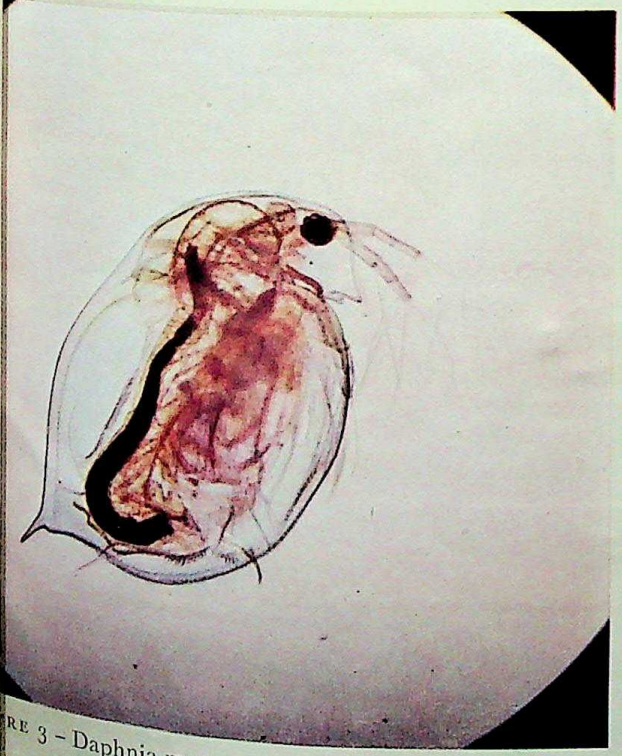
The distribution of haemoglobin in the animal kingdom is rather worrying to zoologists, who like to find everything fitting into a clear genealogical plan, as anatomical structures usually do. All vertebrate animals have haemoglobin; it is common in the *Annelida* (as the earthworm) and the *Entomostraca* (which include *Daphnia*). But why do only one or two of the hundreds of thousands of insect species possess it, as does *Chironomus*, and why only one or two of all the molluscs, as for example the pond snail *Planorbis*? One reason must be that haem, the coloured part of the haemoglobin molecule, is present in most animal cells, whether or not there is haemoglobin in the blood (Keilin [4]). Haem is usually present in cells in very small amounts—so small that it cannot be detected by its colour or be extracted. With pyridine, however, haem forms a compound known as a haemochromogen, with a characteristic strong absorption band easily detected by a spectroscope. In those animals in which the most widely distributed variety of haem, namely protohaem, happens to meet the right protein, globin, haemoglobin may be formed. Haemoglobin occurs in plants too: it is found in the root nodules of beans and peas.

This does not end the spasmodic distribution of respiratory blood-pigments in the animal series. A very few animals have blood which is green. This colour is due to a respiratory protein which Ray Lankester in 1867 called chlorocruorin [5]. The only animals which possess chlorocruorin are certain annelid worms (*Serpulimorpha*) living in the sea. Figures 1 and 5 show photographs of the living animals. The body of the worm is concealed in a protective tube. From one end of the tube projects a beautiful crown of tentacles which serve for respiration and for collecting food. When a small individual is removed from its tube and the blood-vessels are observed through the translucent body with a microscope, the strange appearance is seen of light green blood in the smallest blood-vessels but deep red blood in the larger vessels. Both colours are due to chlorocruorin, for it is a dichroic substance. It appears red when seen in thick layers or in concentrated solution, but green in a thin layer or when dilute. This is shown in figure 7(*d*), which is a colour photograph of the blood of *Sabella*, diluted with water, in a wedge-shaped trough. At one end the chlorocruorin is red, at the other green. Dichroism has a simple explanation, revealed by the spectroscope (see figure 6). When the light passes through a thick layer of a chlorocruorin solution most of it is stopped and only red rays pass (figure 6 (*a*)). With a lesser thickness more light passes, some of which is green and blue (figure 6 (*b*)), the resultant colour appearing green.

Chlorocruorin is chemically nearly related to haemoglobin, although so different in colour. Both are proteins united to haem, which contains iron. Separation of haem from the protein and

RE 1 – Sabella Spallanzanii, *a marine animal with green* cruorin *in its blood. On the left the orange food-catching and* ing *organ is emerging from the tube.*

FIGURE 2 – Daphnia magna, *an inhabitant of pon haemoglobin in its blood.* (× 10)



RE 3 – Daphnia magna *with very little haemoglobin in its*

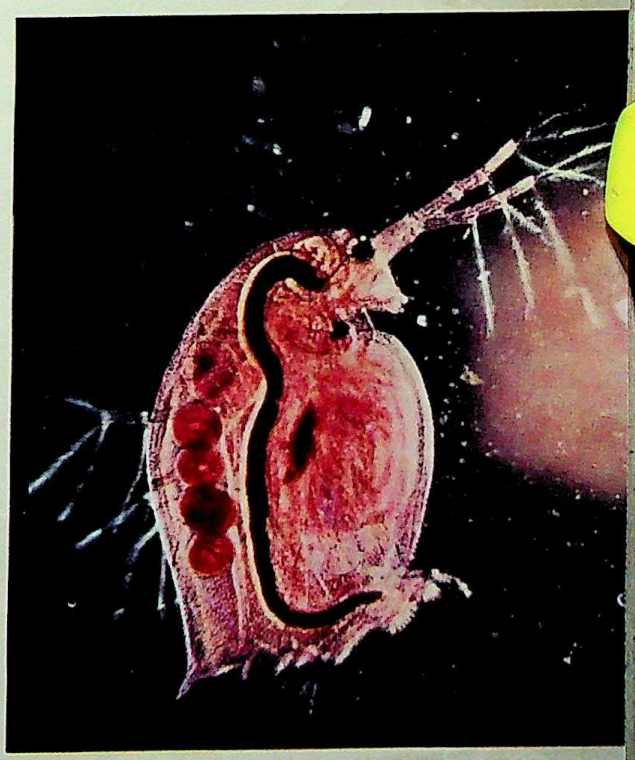


FIGURE 4 – Daphnia magna *carrying in its brood-pou eggs with haemoglobin in them.*

Sabella *and* Daphnia (*figures* 1–5) *were photographed alive.*

RE 5 – Sabella pavonina, *another marine animal with green chloro-*
in its blood.

From C. M. Tonge's The Sea Shore *(Collins), by courtesy of the author, publishers, and Adprint Limited.*]

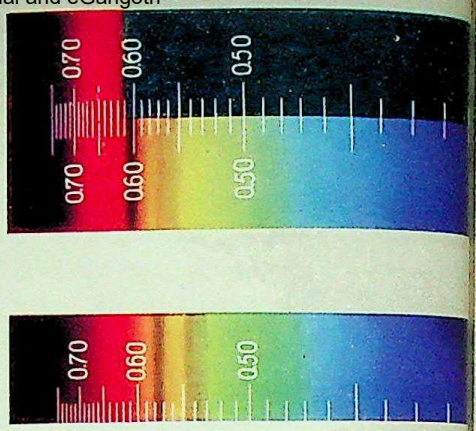


FIGURE 6 – *Absorption spectra:* (a) *concentrat*
of oxychlorocruorin, (b) *dilute oxychlorocruorin*
haemoglobin. Each division of the wavelengt
100 A.

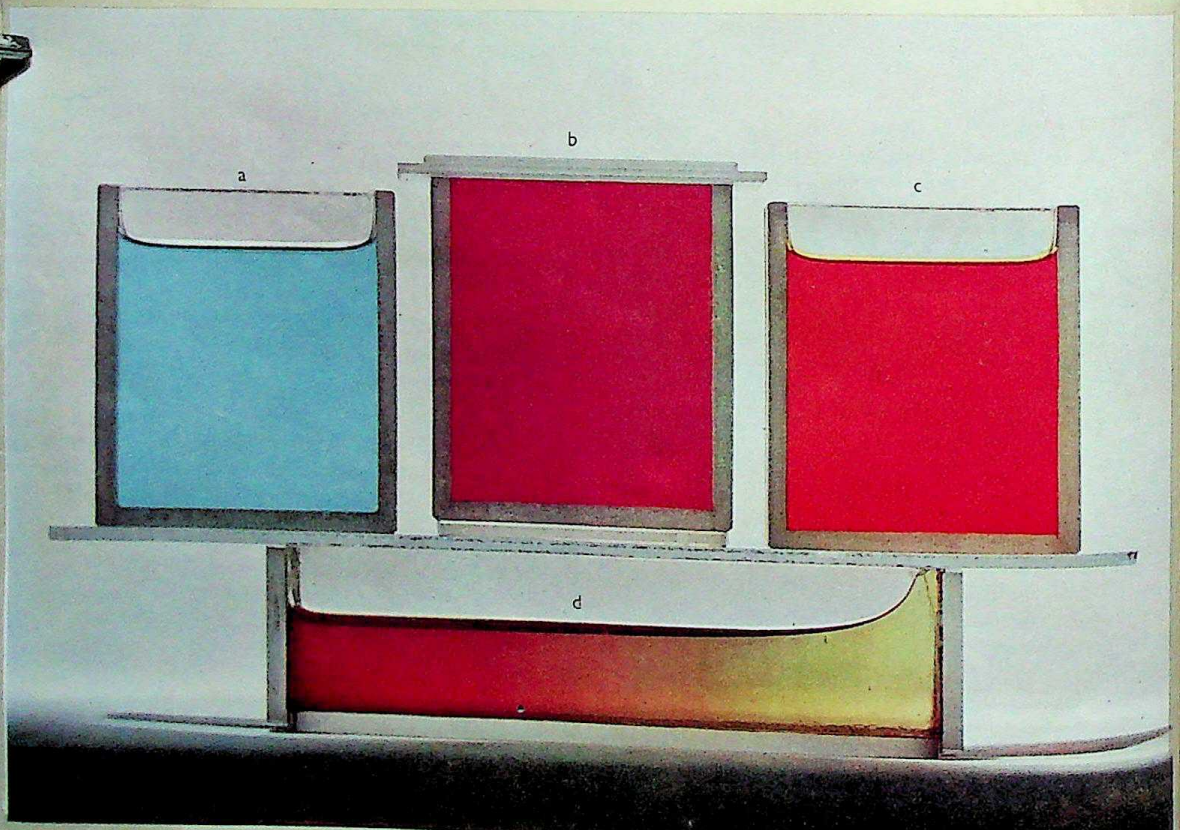


FIGURE 7 – *Bloods of different colours.* (a) *Octopus blood containing oxyhaemocyanin,* (b) *diluted human blood with the haemoglobin deoxygenated,* (c) *diluted human blood with oxyhaemoglobin,* (d) *diluted blood of* Sabella *in a wedge-shaped trough, narrow on the right, showing the dichroism of chlorocruorin.*

removal of its iron atom leaves a porphyrin. The porphyrin of chlorocruorin differs from that of haemoglobin only in one side-chain of one of its four pyrrol rings: here there is an aldehyde instead of a vinyl group (Hans Fischer). Figure 6 shows the absorption spectrum of oxychlorocruorin and the familiar spectrum of oxyhaemoglobin. In the former, as in the latter, there are two bands, but they are of very unequal intensity and are displaced towards the red. Each derivative of chlorocruorin has its characteristic absorption spectrum, corresponding to the haemoglobin series but always with the bands farther from the blue. These spectra have enabled chlorocruorin to be studied in the very small quantities in which it is obtainable. Chlorocruorin is the respiratory blood-pigment of nearly all the serpulimorph annelid worms, with two strange exceptions [6]. *Spirorbis* forms tiny coiled white calcareous tubes on seaweeds and rocks. The blood of one species in this genus contains chlorocruorin, but another species has haemoglobin in its blood in place of chlorocruorin, and yet another lacks either pigment. Nor is this the whole of the bizarre distribution of respiratory proteins among these animals, for *Serpula* possesses both chlorocruorin and haemoglobin together in its blood. There is no other animal known to have two respiratory blood-pigments. No functional reason has been suggested for this duplication.

Chlorocruorin might appear to be a mere biochemical curiosity, a small sideline in evolution, striking perhaps owing to its colour but otherwise unimportant, as it occurs only in a very few marine animals. Yet this is not the case. A substance akin to chlorocruorin is present, not in the blood but in many of the body cells—muscle cells, spermatozoa, etc.—of the majority of animals, including man. Living cells not only have protohaem in them; many contain several haem compounds known collectively as cytochrome (Keilin [4]). The reversible oxidation and reduction of cytochrome is an essential step in the oxidation of carbohydrates, etc., which supplies energy for muscular contraction and other life activities. Cytochrome is composed of three haem compounds, each with a different variety of haem and each with characteristic absorption bands. One of the three components of cytochrome contains the protohaem of haemoglobin. Another has a haem which, although not identical spectroscopically with that of chlorocruorin, is very near to it. The comparison of chlorocruorin derivatives with this cytochrome component has greatly aided its study. Here is a good example of a research, that on chlorocruorin, apparently narrow and academic, which turns out to have wide implications, both in comparative physiology and in medicine, for cytochrome is present not only in man but in bacteria causing human disease.

Haemoglobin, chlorocruorin, and haemocyanin are not the only respiratory blood-pigments. A fourth is known: it is a pink iron-containing protein called haemerythrin, found in a few marine invertebrates (e.g. *Sipunculus* and *Lingula*). There are no colourless oxygen-carrying proteins. I have given the names of the respiratory pigments in the singular, but the plural should really be used, for there are as many varieties of each pigment as there are species of animals possessing them. Specific haemoglobins differ from one another in the exact wavelength of the axes of their absorption bands [7]. Not only do specific haemoglobins exist, but more than one kind of haemoglobin may be found in one and the same animal, for haemoglobin occurs in tissue cells as well as in blood. Meat is red, not only because of red blood corpuscles in its capillary blood-vessels but owing to haemoglobin in the muscle cells themselves. In any one species of vertebrate animal the haemoglobins of blood and of muscle are spectroscopically different from one another. Are there also individual differences? The structural and functional diversity of individual animals and men must in the end be due to individual proteins. Since haemoglobin is a protein, one may ask whether individual haemoglobins can be detected. The answer is yes [8]. Individual rabbits can be distinguished by slight differences in the wavelength of the axis of an oxyhaemoglobin absorption band. The next step was to test human beings, but here the result was disappointing. Although the most diverse types of humanity of both sexes were tested—English, African, Chinese, Jewish—no measurable differences between their haemoglobins could be found.

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Book reviews

THE HUMAN SIDE OF CHEMISTRY

Humour and Humanism in Chemistry, *by John Read. Pp.* 368, *with* 90 *half-tone illustrations. G. Bell and Sons Limited, London.* 1947. 21*s. net.*

The Alchemist in Life, Literature, and Art, *by John Read. Pp.* 90, *with* 29 *half-tone illustrations. Thomas Nelson and Sons Limited, Edinburgh.* 1947. 10*s* 6*d. net.*

Professor Read is to be congratulated upon two excellent books which portray chemists, past and present, as human beings rather than as impersonal automata engaged merely in the collection of facts and the formulation of theories. Both are written, as one has come to expect, in excellent style and with a delicate sense of humour. These books are not only enjoyable reading but, at a time when the dangers of over-specialization are beginning to receive serious attention by educationists, are valuable for cultivating the liberal outlook which seems to have been so important a factor in the greatest scientific advances of the past. It is greatly to be hoped that Professor Read will find time to write more books of the same kind, for he can thus render a most valuable service to the advancement of science.

The Alchemist in Life, Literature, and Art is an analysis of the private lives of alchemists, the information being drawn from such varied sources as Chaucer's *Canon's Yeoman's Tale* and Jonson's play *The Alchemist*, engravings from works on alchemy, and paintings (especially those of David Teniers the younger). The whole is prefaced by a clear account of the principles which guided the alchemists in their work. The publishers as well as the author are to be congratulated, for despite austerity regulations the book is finely produced and well illustrated.

Humour and Humanism in Chemistry deals with a remarkable variety of people and an equally remarkable variety of events. Here we find described such diverse incidents as James IV's philological experiment in the Firth of Forth, Pepys's visit to 'the King's little elaboratory,' and F. J. Stoakley's unhappy experience with the cat and the aspidistra. Particularly interesting are the later sections in which Professor Read writes of the many chemists with whom he has had personal contact, and of his own experiences as a *Doktorand* at Zürich. This is a book which every chemist should read.

CONSERVATION OF PICTURES

The Care of Pictures, *by George L. Stout. Pp. viii* + 125. *Columbia University Press, New York.* 1948. $3.75 *net.*

The conservation of works of art by every available scientific means is a subject of great contemporary interest, but much of this work involves special apparatus unlikely to be available except in large institutions. Mr Stout has now written a book of modest size in which the whole matter is discussed with quite exceptional clarity and charm. Broadly, his aim has been to explain how pictures may be cared for, taking them as structures of a complex physico-chemical nature. Each step in the appropriate treatment is explained with the help of detailed diagrams specially prepared by the author. The use of complicated technical machinery is not assumed, though its role is mentioned fully in an appendix. A number of actual examples are described in order to bring out the specific action of solvents and their powers and limitations. The three-dimensional nature of the problem is kept always in view; restoration and repair (as well as preventive measures) involve operations in depth as well as on the surface. It is clear that many of these processes can be handled only by an expert, which indicates the need for a thorough scientific training at the highest professional level if the task of conservation is to be adequately undertaken. None the less, Mr Stout's book is delightfully readable; it forms the practical basis of the inquiry described in an article in *Endeavour* for July 1948. IAN RAWLINS

HIGH POLYMERS

The Chemistry of High Polymers, *by C. E. H. Bawn. Pp.* 249. *Butterworth's Scientific Publications, London.* 1948. 17*s.* 6*d. net.*

This book is based on a series of post-graduate lectures given in Bristol University in 1946 and is the first publication in this country covering the general principles of common applicability to macromolecules. Before the appearance of this book the student had to depend on the many excellent but highly specialized treatises and review articles which have been published both in America and in Europe during the last ten years. The attempt to cover the many aspects of high polymers in a book of just over 200 pages must inevitably lead to the subject-matter being somewhat condensed, and this applies more especially to the chapters dealing with the kinetics of polymerization and with the solid state, and those readers with no previous knowledge of the subject-matter may therefore find the book rather formidable. However, the student will find no part of the subject neglected, and is guided in his further reading by the extensive and well-selected references given at the ends of the chapters. A most welcome feature of this book is the provision of excellent diagrams, particularly those of molecular structures. J. C. SWALLOW

CURARE

Curare, its History, Nature, and Clinical Use, *by A. R. McIntyre. Pp.* 240, *with several half-tone and line illustrations. The University of Chicago Press, Chicago.* 1947. 27*s.* 6*d. net.*

This book is of a type which an increasing tendency towards specialization is making all too rare. Not only does Professor McIntyre give a detailed account of the chemistry and pharmacology of curare and of its clinical use—fields in which his own work is well known—but he gives also an excellent history of the drug from its earliest description by Peter Martyr. A botanical section gives a full account of all that is known of the ingredients of the various kinds of native curare. The text is accompanied by an exhaustive bibliography, a full index, and a number of good illustrations. The author's own views of curarization and of the possible uses of curare in medicine are of particular interest. The book is timely because of the growing recognition of the therapeutic possibilities of curare; those professionally engaged in this field of research will find it indispensable as a work of reference.

Apart from its intrinsic scientific value curare is a remarkable substance in its history, its method of preparation, and its properties. This scholarly and well-composed account of the poison should prove of interest to all scientists, whether or not they have a direct professional interest in curare.

ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

VOLUME VIII APRIL 1949 NUMBER 30

Pierre Simon de Laplace, 1749–1827

Though, after the appearance of the *Principia*, the Newtonian theory of gravitation was enthusiastically accepted in England, mathematicians on the Continent of Europe were unanimous in their hostility. They preferred the theory of Descartes, which attempted to explain the motion of the bodies of the solar system by a combination of vortices. The general diffusion, in France and beyond, of the doctrine of gravitation was due primarily to Voltaire, who in 1738 published a lucid and popular account of Newton's discoveries; this small work was widely read and paved the way for the general acceptance of the Newtonian theory. Newton himself had developed it in its broad outlines, but the task remained of proving that it could account in detail for the motions of all the bodies in the solar system. During the eighteenth century Newton's own countrymen contributed little to this task; its performance was left to a group of brilliant Continental mathematicians—Euler, Clairaut, D'Alembert, Lagrange, and Laplace. Their work was made possible by the researches of Leibnitz and of the two Bernouillis in the development of the new differential calculus, which provided them with a powerful analytical tool. The neglect of these methods in England was the result of the estrangement between British and Continental mathematicians, which developed from the unfortunate quarrel between Newton and Leibnitz.

The most important share in the great task was taken by Pierre Simon de Laplace, who was born two hundred years ago on 23rd March, 1749. Laplace has appropriately been called the Newton of France. He took as his life's work, from which he never deviated, the detailed application of the Newtonian law of gravitation to the entire solar system. He had to work out the effects of the mutual gravitational perturbations of all the members of the Sun's family of planets on each other and on the Sun. The first great question which required an answer was whether the cumulative effect of these perturbations could become sufficiently large to render the solar system unstable. Important contributions to this problem were made by Laplace and by his equally great contemporary, Joseph Louis Lagrange, but the final step was taken by Laplace, who proved that, whatever the relative masses of the planets, the inclinations and eccentricities of their orbits, if once inconsiderable, would always remain so, provided the planets all revolved round the Sun in the same direction. The solar system is therefore stable.

Between Lagrange and Laplace there was an essential difference. Lagrange valued elegance and generality of treatment; a particular problem was the occasion for the application of a general method. Laplace, on the other hand, used mathematics as a tool, which he modified to suit each special problem in the pursuit of his single central objective. The work that he did in fields other than celestial mechanics was done because new tools were needed to deal with some of his problems.

It was in this way that Laplace came to develop the theory of the potential function, a concept which shows the inspiration of genius. Even if Laplace had done nothing but this he would still be justly ranked among the immortals. The introduction of the potential function was one of the biggest strides ever taken in mathematical physics. With Laplace's coefficients it provided a powerful calculus for an attack on the physical problems of fluid motion, of elasticity, of the conduction of heat, and of electro-magnetism. From it has developed one branch of the mathematics of boundary-value problems. Laplace himself introduced the potential primarily to deal with the attractions of spheroids and the figures of the planets.

Laplace's investigations in pure mathematics, such as the reduction of the solutions of linear differential equations to definite integrals, and his

solutions of linear partial differential equations of the second order, were undertaken for the same purpose. So also was his epoch-making work on the theory of probability, which was essential for dealing with large numbers of observational data.

The contributions of Laplace to the subject of gravitational astronomy are too numerous to record in detail. He did more than lay the foundations of celestial mechanics; he built practically the whole edifice, leaving relatively little to his successors. He worked out in great detail a new treatment of the lunar theory; he provided the explanation of the secular acceleration of the mean motion of the Moon, which had defied the attempts of so many astronomers; he developed the theory of periodic and secular perturbations of planetary and lunar motions; he accounted for the long inequality of Jupiter and Saturn—which appears as a slow alteration in their rates of motion—as arising from the near commensurability of their mean motions; he investigated the figures of equilibrium of a rotating fluid; he developed the theory of the figure of the Earth; and he made improvements in the theory of the tides.

All these results were collected together, and co-ordinated with the results of his predecessors and contemporaries into a reasoned whole, in his great work, the *Mécanique Céleste*, which appeared in five volumes between 1799 and 1825. In it, the theory of the planetary system is presented in a state of almost complete development. The remaining discrepancies between observation and theory were small in comparison with those which had been removed. The treatise is difficult to read because the mathematical exposition is extremely concise; the frequent remark '*Il est aisé à voir*' must not be taken literally.

Laplace was almost as great a writer as a mathematician. His celebrated treatise had been preceded in 1796 by a popular account of the main results, the *Exposition du Système du Monde*. In this charmingly written work there is neither a single diagram nor an algebraical formula; the exposition is lucid and straightforward. It was in the last appendix to this work that he advanced his famous nebular hypothesis of the origin of the solar system, for which he is best known outside the circles of professed astronomers and mathematical physicists. Laplace drew attention to certain remarkable characteristics of the solar system, from which he inferred that the system could not have originated by chance. He suggested that it had been formed by condensation out of a nebula, and he sketched a process by which, if endowed with rotation, the latter might, as it contracted, throw off a series of rings which in turn might condense into planets, with or without satellites. The theory in this form is untenable, because of difficulties about angular momentum; various modifications have been attempted, none of which is entirely free from objection. There is today still no satisfactory theory of the origin of the solar system. Laplace referred to the details of his hypothesis as 'conjectures which I present with all the distrust which everything that is not a result of observation or of calculation ought to inspire.' It is not his fault that many of the expounders of his nebular hypothesis have taken it more seriously than did he himself.

The long non-mathematical introduction to his other great work, *Théorie analytique des Probabilités*, shows the same clarity of style as the *Exposition du Système du Monde*. It was the quality of his writing which gained for him the distinction, unusual for a mathematician, of election as one of the forty 'immortals' of the *Académie Française*.

In the personality of Laplace there were elements that we cannot admire, but in scientific matters he would not compromise, and he was both honest and courageous in upholding his opinions. His work had a profound influence on the development of science in the eighteenth century. In his estimate of his own work he was modest, and his last words are reported to have been '*Ce que nous connaissons est peu de chose; ce que nous ignorons est immense.*'

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Genetic particles

C. D. DARLINGTON

In recent years the chemical approach to the study of genetics has proved an increasingly valuable supplement to the organismal one. Much progress has been made towards identifying the various particles—apparently self-propagating proteins—which determine genetic processes; towards locating these particles in different observable structures in the cell; and towards discovering their relative importance in respect of heredity, development, and infection.

It is obvious to us, although it was by no means obvious to the fathers of biology—Darwin, Mendel, and Pasteur—that the property by which like begets like in organisms must rest on a similar property among certain of their molecules. At a molecular level there must be determining particles owing their property of determination to a high activity and a capacity for self-propagation.

These determining particles were already becoming chemically identifiable within the germ cells when Miescher, in 1871, discovered nucleic acid, and a contemporary philosopher, Engels, was able to speak of life as 'the mode of activity of proteins.' But, in fact, it is only during the last fifteen years that we have been able to sort out the different kinds of determinant, to allocate them to different parts of the cell, and to assign them to the different modes of propagation and degrees of permanence that we describe under the names of heredity, development, and infection.

During the nineteenth century it had already become clear that most of the important structures and all the important changes recognizable as essential to life were bound up with proteins—hence the definition just given. During the last fifteen years it has become clear that the proteins essential to growth, i.e. to the formation of new proteins, are bound up with the nucleic acids.

THE NUCLEUS

The nucleic acids or their precursors can be recognized in cells by their differential reactions to enzymes, stains, and ultra-violet light. They occur almost exclusively in proportion to the activity of the cell in protein production. The highest concentrations are thus found in the eggs, and in the meristematic and tumour cells, whether of plants and animals. Leucocytes, and the tissues of rapidly growing young embryos, which have been producing proteins to the limit, are starved of nucleic acid. An experiment of Caspersson's confirms the evidence. Yeast (whether it is fermenting or not) in the absence of a source of nitrogen is starved of nucleic acid. But, when protein production becomes possible, its stock is at once restored.

The meaning of this primary function of the nucleic acids appears when the structures of cells are chemically described. Cells contain a variety of self-propagating particles, all of which seem to consist of proteins in association with nucleic acids. Outside the nucleus these particles contain nothing but the *ribose* form which is associated equally with the plastids of plant cells, with the large microsomes that Claude has separated from animal cells, and with the smaller viruses.

Inside the nucleus there is also ribose nucleic acid. In addition, attached to the chromosomes, especially during mitosis, is its *desoxyribose* relative. This molecule is the king-pin of cell-multiplication and heredity. By its capacity for indefinite polymerization, probably in columns of variable spiralization, it is responsible for a large part of the active performance of the spiralizing chromosomes at mitosis (figure 9). It is also probably the agent of their multiplication (figure 11). It maintains their specificity and, as in transforming *Pneumococcus*, it can even impose a new specificity. But in protein production, as opposed to self-propagation, the decisive part is played by the cytoplasmic form, the ribose nucleic acid, of which active protein-producing nuclei keep large quantities stored in a special body, the *nucleolus* (figure 10).

The activities of the chromosomes in protein production are laid out in a diagrammatic way, as Caspersson has shown, in the two kinds of chromomere-producing nuclei: in the salivary gland nuclei of flies and in the meiotic nuclei at the beginning of the germ-cell-forming divisions. The genes in these nuclei are charged with nucleic acid but are engaged in protein production. The successive genes acting as units thus push one

another apart on the chromosome string. They then come to appear like beads on a thread, of unequal size and unequally strung together (figure 10).

In the salivary gland nuclei of *Drosophila* two kinds of chromomere can be made out. There are large ones which produce large proteins and have strong pairing affinities for their opposite numbers in the partner chromosome, and there are small ones which produce small proteins and have weak affinities. The first, which comprise what is known as *euchromatin*, contain all the genes with highly specific mutations. The second, which comprise the *heterochromatin*, were long believed to be inert but are now known to contain those genes which Mather describes as polygenes, whose mutations have a slight and repetitive effect.

In view of the parallel distinction between two kinds of chromomeres and two kinds of gene mutations it seems likely that size, specificity, and complexity are related both in the gene and in its products. In this case a succession of small chromomeres would be due to *replication* of similar elements, and the formation of large ones to *integration* of dissimilar elements, somewhat in the following way:

—o—o—o—o—o—	—omxox—
—x—x—x—x—x—	—xmxom—
—m—m—m—m—m—	
Heterochromatin (*small chromomeres*)	*Euchromatin* (*large chromomeres*)

In many plants and animals the heterochromatin can be specifically starved of nucleic acid by allowing nuclei to undergo mitosis below freezing point. It then appears as unstained blocks in the metaphase chromosomes (figure 11; *cf.* ENDEAVOUR, Vol. 1, 1942, p. 105). Further, a general or unspecific nucleic acid starvation—or its opposite, a surfeit—occurs normally in all organisms as a process of differentiation. In the bone marrow cells of mammals, for example, the white blood corpuscle precursors, as La Cour found, are starved and the red surfeited. This differentiation is exaggerated in pernicious anaemia, so that a cancer-like condition of the red precursors is induced. The sticky chromosomes and many-poled spindles produce daughter cells with defective nuclei which cannot live (figure 7).

The functions of chromosomes and genes in protein production are the basis of almost the whole of genetics and cytology and almost the whole of biological permanence. No one doubts that their continuity, their specificity, and their balance underlie the continuity, the specificity, and the balance of heredity in all the higher organisms. Outside the nucleus we have been, until recently, on much more uncertain ground. It is this ground that we must now explore.

CENTROSOMES AND CENTROMERES

A *Paramecium* which has been deprived of its gullet cannot reconstruct it. There must thus be genetic determinants in the cell which are invisible but none the less irreplaceable. Under the microscope we can make out three varieties of visible body with some kind of continuity. First, there are the organelle-forming bodies of single-celled forms of life. These, especially the ones attached to flagella and other organs of movement, are chiefly fibre-secreting bodies. Some of them can be seen to divide when the organism divides.

The second type of body is the centrosome, or spindle organizer, found in animals and lower plants. This body is also concerned with the secretion or arrangement of fibres. It organizes fibrous cell proteins to form the spindle whose liquid-crystal structure permits the regular and polarized movement of chromosomes when the nucleus and the cell divide at mitosis (figure 1). The centrosome propagates itself (figure 2). It is brought into the egg (which loses its own centrosome) by the sperm, and when two sperms enter the same egg a spindle with three or four poles is formed.

Spindles are normally formed in conjunction with the chromosomes. Do they indeed require the chromosomes to help in organizing them and to keep their centrosomes multiplying? In the newt *Triton taeniatus* Fankhauser has tested this possibility. He split the egg with a thread and allowed the half without a nucleus to be entered by a single sperm, the nucleus of which then divides to give haploid nuclei and cells. The centrosomes of these cells, however, split out of step with their nuclei, and cells are found dividing with the wrong number of centrosomes and consequently having the wrong number—one, three, or four—poles to their spindles. These give rise in due course to daughter cells lacking chromosomes of the haploid set, and some indeed without any chromosomes at all. At an early stage of development, when nothing new is being produced, such cells can continue to live and may divide a few times. Fankhauser's experiment thus shows that the centrosomes can divide in cells without nuclei or chromosomes. It shows that the centrosome is genetically self-sufficient and entirely capable

alone of arranging fibrous proteins so as to form a spindle.

In the higher plants there are no centrosomes, and the spindle is organized by the chromosomes alone. A special organ known as the centromere is responsible. The centromere is active, secreting or organizing the spindle fibres, during mitosis. When all the other genes are coated with nucleic acid it alone remains naked. At the end of this activity it suddenly splits, to pull the daughter chromosomes apart towards opposite poles of the spindle it has organized. Metaphase is followed by anaphase (figure 1). It seems as though the centromere cycle on the spindle, like the ordinary gene cycle inside the nucleus, is due to a change from production to reproduction. The difference in the timing of activity of gene and centromere goes with a difference in the timing of nucleic acid charging.

Where the centrosome and the centromeres are both present they work together, and it is difficult to distinguish their activities except by their positions—inside and outside the nucleus. There is even some particular evidence in the sperm formation of molluscs that the centrosome is nothing more than a disembodied centromere liberated in the cytoplasm a very long time ago and unchanged ever since.

We might expect a cytoplasmic determinant to be capable of varying degrees of aggregation. In view of the analogy between centrosomes and centromeres it is therefore interesting to note that the centromere is an aggregation. Normally it splits lengthwise to give equal and legitimate daughters. Abnormally it can split crosswise. It then gives unequal and illegitimate daughters—illegitimate because in arising they break the chromosome in half and give two new shorter chromosomes with terminal centromeres of reduced size. These new fragment centromeres are sometimes capable of doing the job of their parent centromere, which must therefore have arisen by the replication of a smaller unit. It is a multiple gene. No doubt the replication has been allowed to go far enough to give the best-adjusted mechanism.

It is fundamental for our understanding of genetic particles to know how this misdivision of a centromere takes place. Nuclear genes can organize proteins in two directions. Normal action must be perpendicular to the axis of the chromosome. When chromomeres are produced, action is along the axis of the spindle. The centrosome, on the other hand, acts radially in all directions to give an aster before the spindle develops. The centromere, we now see, can act in two alternative directions. In its normal division its propagation has followed the normal direction of its action, perpendicular to the chromosome axis. In its misdivision it is unable to propagate itself and its action is then twisted through a right angle, so that the fibres it secretes rend it asunder into two parts (figure 12, p. 59).

PLASTIDS

The third type of genetic body visible in the cytoplasm is the plastid responsible for the development of chlorophyll in green cells. In the algae and protista the plastids demonstrably arise only from pre-existing plastids; they are often fixed in number and their physiological properties can be studied in a variety of ways. For example, the flagellate *Euglena gracilis*, with a favourable supply of peptone broth, multiplies faster than its own plastids, so that (as was suggested in 1912 by Ternetz) there is in the end only one plastid to be divided among two daughter *Euglenae*. One of them has to go without. In this way an irretrievably white race is brought into existence.

In the higher plants the visible continuity of the plastids is hard to show: small and colourless as they are, and not differentially stainable, they are too inconspicuous in the embryonic cells. By experimental breeding, however, they have been made to reveal a marvellous repertory of genetic properties. Indeed, they reveal all those foundations of the physiology of permanence which have not already been disclosed by the chromosomes themselves.

The simplest condition is shown by the comparison of two kinds of chlorophyll defect in the Chinese primrose. One is strictly Mendelian in its recombinations: *AA*, *Aa*, and *aa* are green, yellow, and white respectively. The yellow is short of chlorophyll but can live. The white or albino almost totally lacks it and dies as a seedling. Thus these differences in plastid action are strictly under nuclear control—to be precise, they are due to a single gene change.

The second defect is seen in a yellow-leaved form of the same species, all of whose progeny are yellow like itself—no matter whether it is self-pollinated or crossed with a green plant. The inheritance is solely through the eggs. It is matrilinear. Some determinant is carried by the eggs which is not carried by the pollen. What is this determinant? The answer was provided quite clearly by Erwin Baur's experiments with the

zonal pelargoniums in 1909. Many of these ornamental plants are variegated. They consist of fairly stable combinations of green and white tissue, in which the cells without chlorophyll form a regular skin over those with chlorophyll, or *vice versa*.

Occasionally mixed green and white plants—chimaeras, as they are called—sport a shoot which is wholly green or wholly white. A white shoot is of course parasitic on the rest of the plant. Either of these pure shoots will breed true if its flowers are self-fertilized. But a white shoot can also be crossed with a green shoot reciprocally, i.e. both white eggs with green pollen and green eggs with white pollen. Again, some of these crosses show a purely Mendelian inheritance; that is to say they display a second generation segregation of the alternative types. Others show something different—a first-division segregation. Green, variegated, and white seedlings appear together from the cross. Moreover, the variegated seedlings develop by the emergence of green and white sectors of tissues sometimes as early as in the cotyledons (figures 5 and 6). Baur's explanation was that the plastids were responsible for their own inheritance. They were autonomous, but they were brought into the fertilized egg by the pollen as well as by the egg itself. Inheritance, although not Mendelian, was thus still biparental. The mixed cells in the embryo could then, by random distribution of the green and white plastids, give some purely white, and some purely green, cells and tissues.

When the numbers of green, white, and mixed seedlings are counted in the progeny a further remarkable fact appears. There are more white seedlings from the green mother than from the white. Not the maternal but the paternal side seems to prevail in inheritance, as is shown in the table.

Results of reciprocal crosses between green and white shoots in Pelargonium; *from Baur* (1909) *and Chittenden* (1925)

♀ × ♂	Total	Green (per cent.)	Variegated (per cent.)	White (per cent.)
G × W	280	77	13	10
W × G	93	72	28	·0

So deeply has it been felt necessary for non-Mendelian inheritance to show a reciprocal difference in favour of the egg-parent that no one has ever noticed the lack of any maternal predominance in this, the classical example.[1] It is no doubt possible for pollen to contribute more than the eggs, but in this case that need not be assumed. It will be noticed that the proportion of variegated seedlings is higher with the white mother, and also that the white mother's fertility is heavily reduced (for the reciprocal crosses were probably in equal numbers). Rather it seems therefore that, on the green mother, we get a complete survival of the embryos and hence an unimpaired ratio of types. On the parasitic white mother, with poorer nutrition, the fertility is reduced no doubt by the elimination of most of the less viable embryos—those 200 or so which should have arisen with white plastids only.

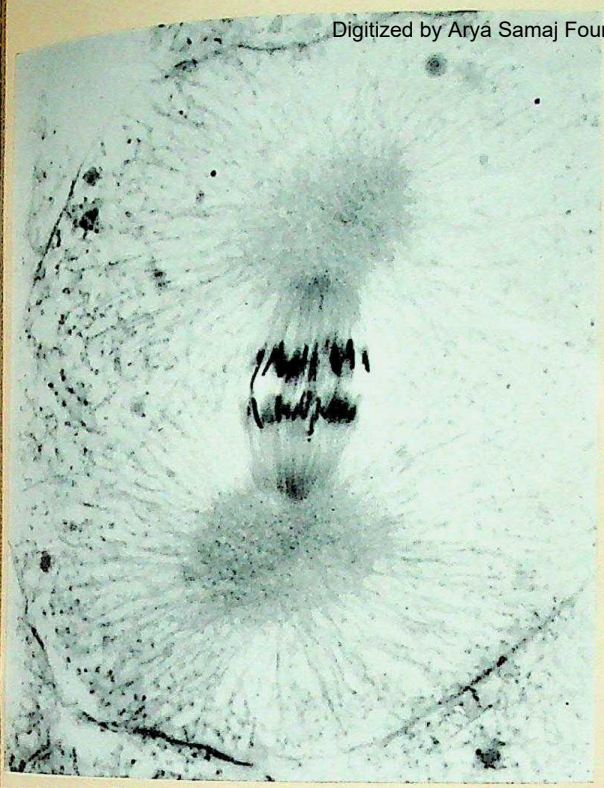
The origin of the variegated chimaeras in *Pelargonium* became clear much later from studies of species crosses in *Oenothera*, the evening primroses. Here Renner found that reciprocal crosses often differed in plastid character. The plastids were largely transmitted through the egg; only a trace came over in the pollen tube. The plastids of one parent were colourless in the hybrid, while those of the other were green. Thus, if we label the nuclei and the plastids *A* and *B* according to the species they come from, we can make out the following scheme:

Cross	*Nucleus*	*Plastids*
A♀ × *B*♂	*AB*	White (*A*) + trace of green (*B*)
B♀ × *A*♂	*AB*	Green (*B*) + trace of white (*A*)

The whites with a trace of green die. The greens with a trace of white live and sort out their plastids as in *Pelargonium*: sometimes they give wholly green shoots and less often wholly white ones. From such crosses many variegated plants known in horticulture may have arisen.

An important question now arises. Are the white *A* plastids white because the strange *AB* nucleus has made them change their genetic character, or mutate as we may say? Or have they changed their appearance and activity merely for the time being, and because the *AB* nucleus is keeping them starved? When eggs with *A* plastids from white shoots on the mixed plants are crossed back with pollen of the *A* father, half the progeny have *AA* nuclei. They are green

[1] Baur added his reciprocal classes together and Chittenden did not add up his classes at all. Neither gives the numbers of flowers pollinated.



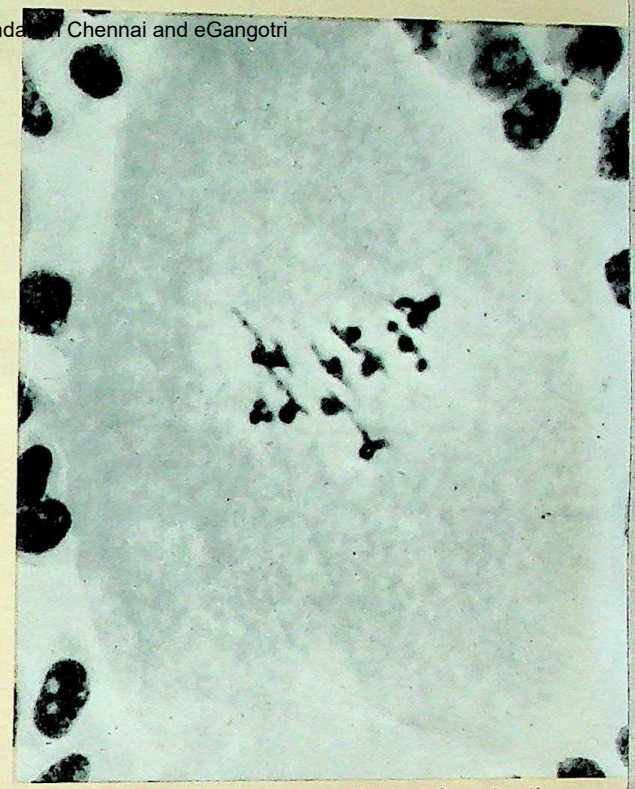
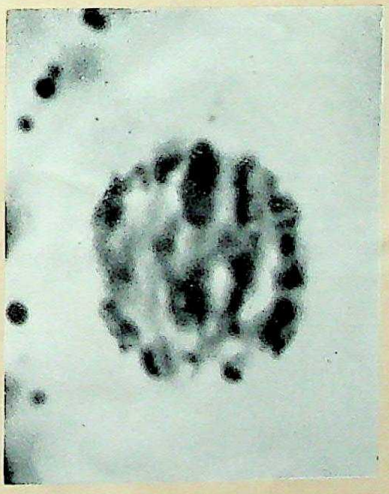


FIGURE 1 – *The arrangement of the mitotic spindle in large cells.* (*Left*) *White fish egg cleavage division, from Darlington and La Cour,* 1947 (× 3,600); (*Right*) *embryo sac of a lily,* Fritillaria pudica, *with no centrosomes and a skew spindle formed by the centromeres* (*acetic lacmoid preparation*). (× 800) *(Photographs by P. C. Koller and L. F. La Cour.*

FIGURE 2 – *Meiosis in a spider,* Tegenaria domestica, *showing the division and movements of the daughter centrosomes and their formation of the spindle at meiosis, from Revell,* 1947. a–c *prophase,* d *metaphase,* and e *anaphase.* (× 3,200)



a

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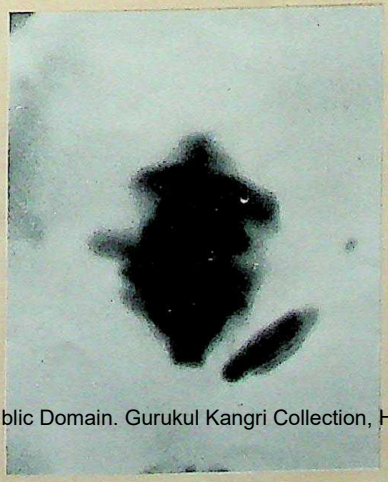

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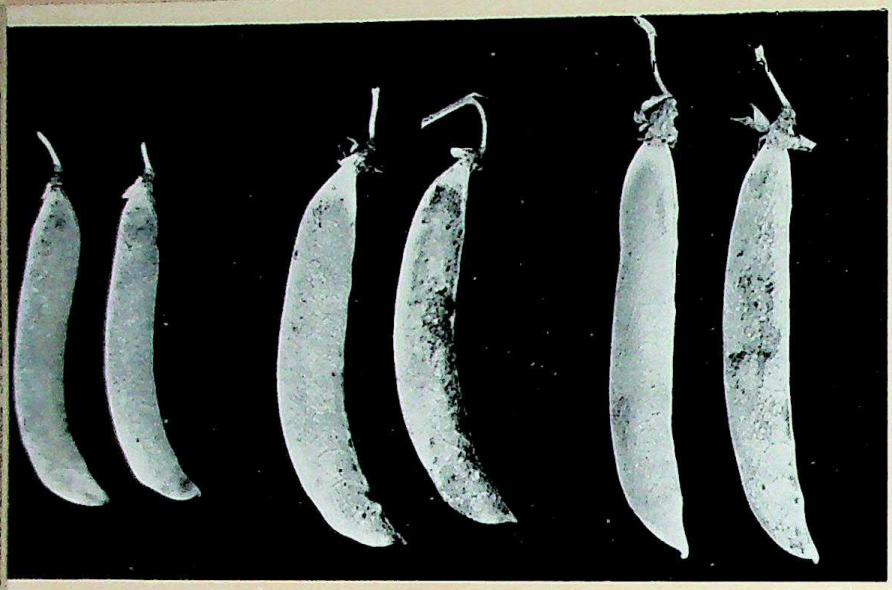

FIGURE 3 – a *and* b, *Pods*
leaves of rogue (left), intermed
and type (right) peas of the va
'Early Giant'; c, a leaf of an
mediate plant which is rogue o
left and type on the right side o
to a sorting out of plasmage
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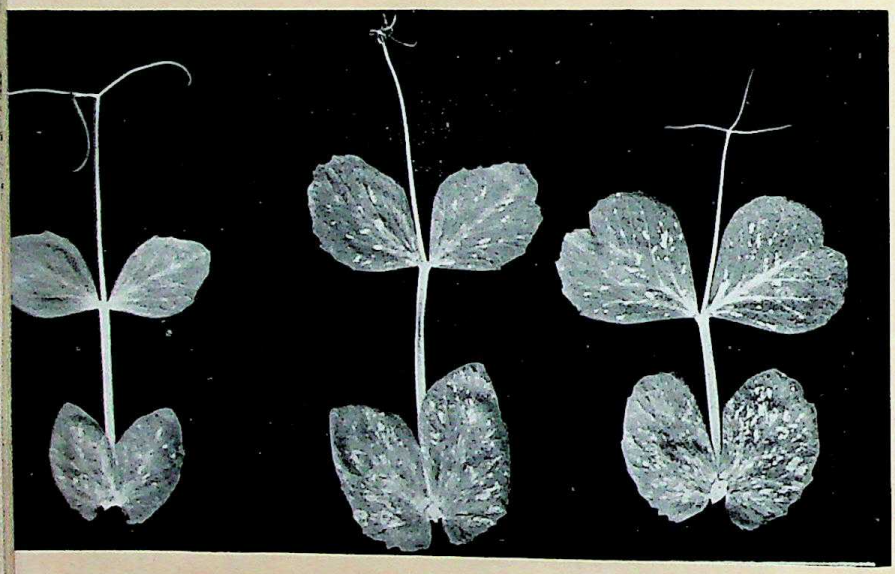

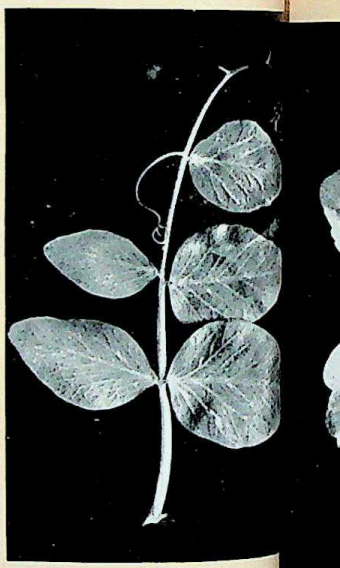

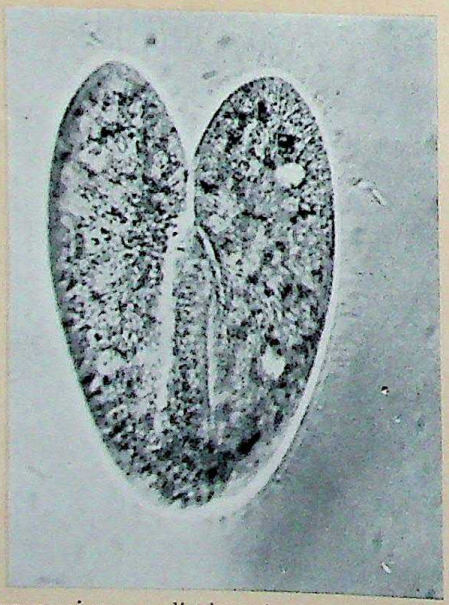

IGURE 4 – Paramecium aurelia *in conjugation. (Left) (Living preparation with visible cilia), normal mating, showing the*
pping gullets. Only the micronuclei are being exchanged. (Right) (fixed and stained preparation), later stage, with artificially
paration; a broad band joins the two mates and permits the exchange

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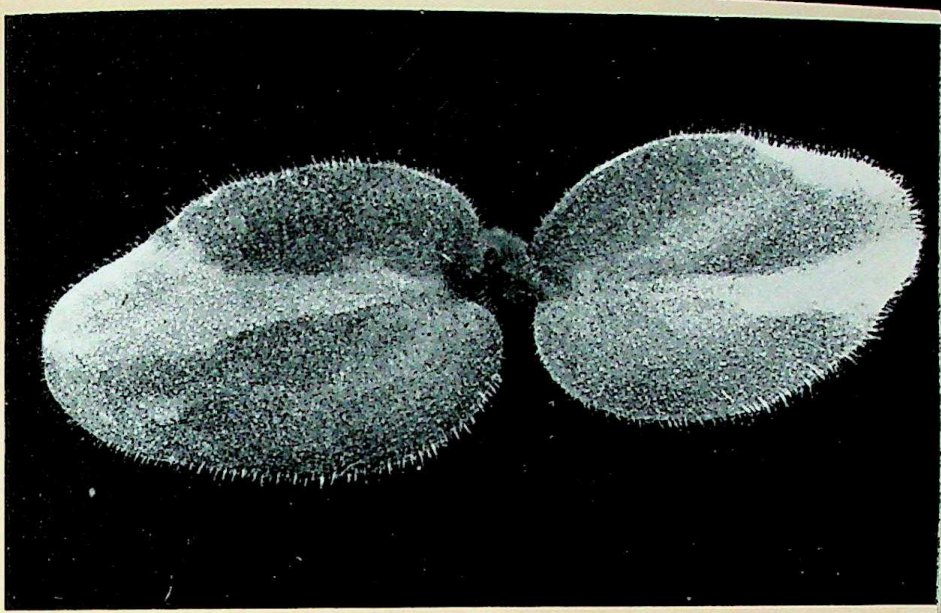
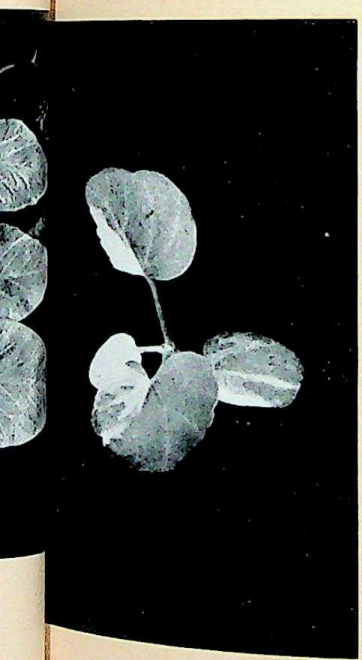
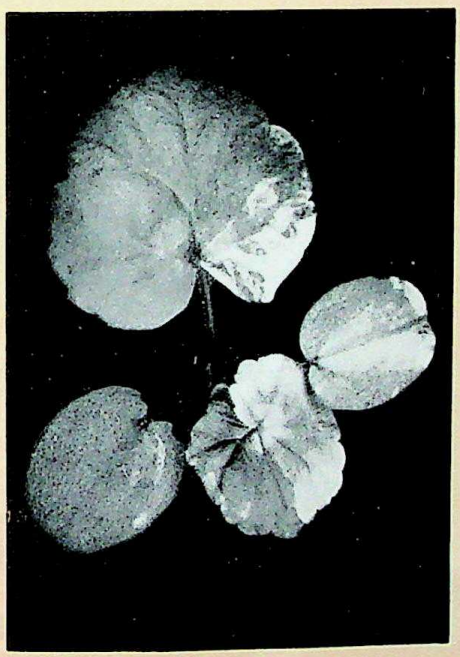
IGURE 5 – *Seedling of zonal* *elargonium, green × white, show-* *g the separation of green and white* *ssues in the cotyledons owing to* *sorting out of plastids in cell* *vision. Bateson (unpublished).* × 6)



IGURE 6 – *Seedlings as in figure* *at a later stage of development.* *Approximately natural size.)*





a

b

IGURE 7 – *Mitosis in the precursors of the white* (a) *and red* (b) *blood cells in the bone marrow of a man with pernicio* *anaemia. The exaggerated differentiation in nucleic acid charge and protein production gives a multiple spindle in one and* *Evans, La Cour, 1944.* (× 2,400)

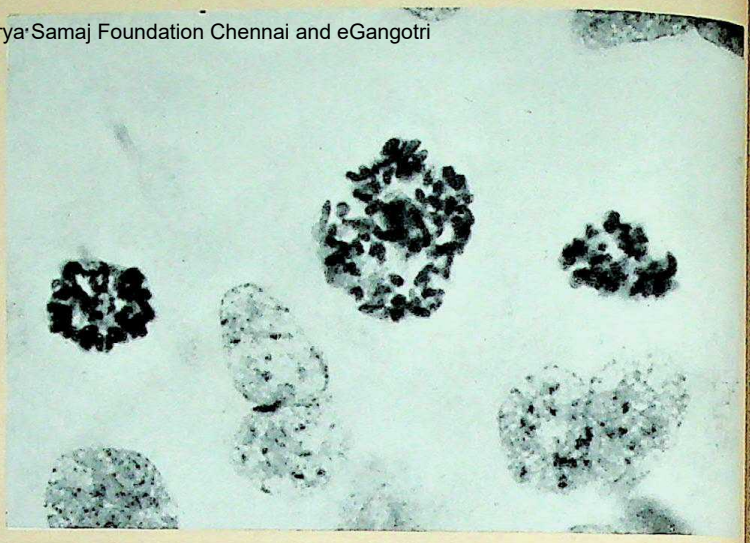
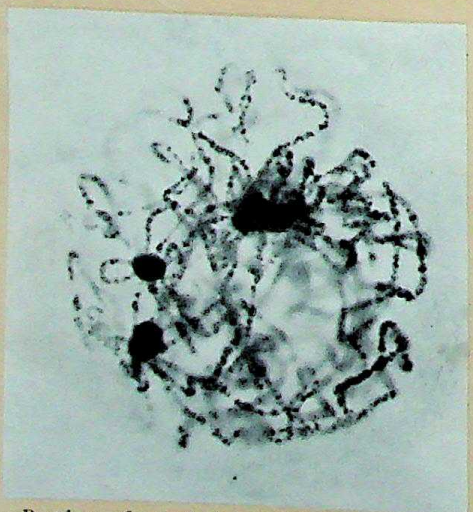


FIGURE 8 – (*Left*) *Multiple spindle in a dividing cell of carcinoma of the cervix of the womb.* (*Right*) *Polyploid cell resulting from such an abnormality side by side with diploid cells.* (× 3,000) (*Preparations and photographs by P. C. Kolle*)

IGURE 9 – *The chromosomes at the first division of meiosis in the pollen mother cell of a triploid* Tradescantia *with each x chromosomes represented three times. They are partly in threes and partly in twos, with the third unpaired. The sexual cells or ga ill have various numbers of chromosomes, from six to twelve. The even triploid balance is maintained in all the vegetative cells lant by the regular division of the chromosomes at mitosis: there is no sorting out except at meiosis.* (× 1,300) (*Acetic lacmoid preparation and photograph by G. Ro*



IGURE 10 – *Prophase of meiosis in pollen mother cell of* Fritillaria ecurva, *showing the chromomere structure of the paired chromosomes. The arge dark bodies are blocks of heterochromatin*

FIGURE 11 – *Anaphase of mitosis in* Tri grandiflorum, *showing failure of gene reprod*

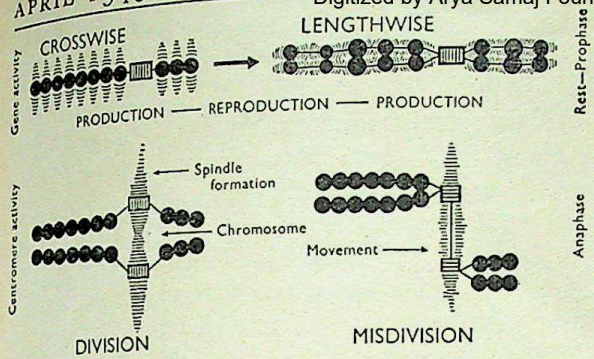


FIGURE 12 – *Protein production and orientation.*

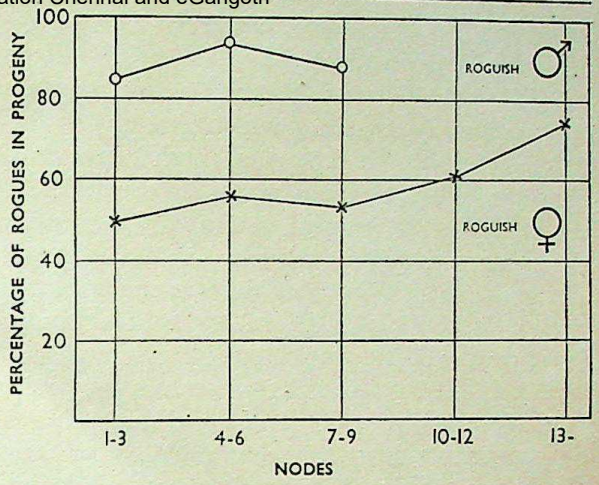


FIGURE 13 – *Graph showing (i) the preponderant effect of the male gametes in the inheritance of the rogue character in reciprocal crosses of intermediate rogues and types in the pea; and (ii) the increase in the proportion of rogues in the progeny of the higher nodes which show the rogue character most strongly. Extracted from the data of Bateson and Pellew,* 1920.

again. Evidently their plastids have not mutated.

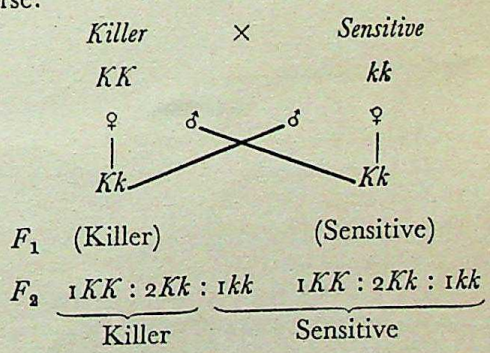
Plastids can, however, mutate in the species and hybrids of *Oenothera*. Indeed, they can probably do so in all species of green organisms, including *Euglena*. They mutate not as a mass change of all plastids but as a change of individual plastids sporadically during development. Their change has then the same apparent and spurious indeterminacy as the mutation of genes and the breakdown of radium atoms. Special nuclear genes have, however, been found in barley, rice, and maize which cause the plastids to mutate frequently enough to give a regular variegation and a noticeable frequency of white seedlings.

Part of the character of plastids which they retain, according to Renner, in combination with various nuclei, consists in a characteristic rate of propagation (irrespective of whether it is green or white) in relation to a given nucleus. Naturally there is a limit to the number of plastids any cell will hold, so that with variable rates of multiplication there must be competition among the different plastids in a mixed cell. Renner in fact found that in his *Oenothera* crosses the conditions of this competition between pairs of plastid types varied under different nuclei.

PLASMAGENES

The continuity and permanence of plastids now seem to justify us in attributing to their nucleo-protein determinants a similar structure and a similar name to that of nuclear genes. They are known as *plastogenes*. Their great importance is in the guidance they give us in entering the otherwise uncharted field of the cytoplasm. Can it be that similar determinants—*plasmagenes*—exist there, unattached to large and labelled products like the plastids and the chromosomes, but nevertheless of permanent physiological importance?

This is what the work of the last ten years has established. In *Paramecium aurelia*, Sonneborn, by a remarkable series of experiments, has discovered that a capacity for killing other animalcules is derived from certain *kappa* particles in the cytoplasm. These particles depend for their propagation on the production of a necessary precursor substance by a nuclear gene, *K*, which is absent from some strains. Thus a cross between a killer and a non-killer strain of *Paramecium* may take the following course:



Thus the killer property is restricted to the female line. It is also restricted to the animals carrying a *K* gene. This means that the *kappa* particles cannot be made by the nucleus alone or by the cytoplasm alone.

In *Drosophila melanogaster* a remarkably instructive plasmagene has been thoroughly tracked down by the work of L'Héritier. It is the CO_2-sensitivity 'genoid.' The genoid is predominantly inherited through the mother. It is also (unlike *kappa* or the plastids) an adaptively neutral or, as we might say, futile variation: the question as to

whether a fly is sensitive to carbon dioxide or not cannot arise in nature.

The *Drosophila* and *Paramecium* plasmagenes show two properties in common that are of profound significance. They are both capable of infection. When two animalcules are persuaded to stick together too long in mating, one can infect the other with *kappa* particles. Again, the serum of a sensitive fly, injected into a non-sensitive, will endow the fly's eggs with transmitted sensitivity: in other words, the particle is diffusible and artificially infectious. It is not, however, naturally infectious, and it is this which distinguishes a plasmagene from a neutral virus. The virus of 'breaking' in tulips has remained in equilibrium in certain vegetative clones for hundreds of years, doing them no harm. It is neutral, but it is transmitted naturally by an aphid and is therefore a true virus. Such true viruses must often have arisen in the recent or remote past by transplantation or mutation of self-propagating proteins in the cell.

The second common property of *kappa* and the genoid is that of showing a limited rate of propagation in the cell. When the parent (or host, shall we say?) organism is grown at a high temperature its cells can be made to multiply more quickly than their plasmagenes. It grows away from them just as *Euglena* may grow away from its plastids.

Before we follow up this clue there is yet another primary problem connected with the plasmagene that we must look into, viz. that of development. In many plants, abnormalities of development are known which are transmitted to all progeny as though by a virus. Of these hitherto mysterious misfits the most remarkable is the rogue character of various cultivated plants. In peas, the rogue appears as a narrow-leaved mutant in most of the broad-leaved varieties. In mutants of one variety, viz. Sutton's 'Early Giant,' Bateson and Pellew found that the rogue character developed gradually as the plant grew, reaching an extreme at the top. Further, they found that such roguish plants gave a higher proportion of rogues from the top parts, where the leaves were narrowest. Finally, what was most astonishing (and indeed, at the time, disconcerting), in reciprocal crosses with normal plants the pollen carried the rogue character more effectively than did the eggs (figure 13).

An explanation of all these properties is now almost self-evident. The rogue character is determined by a plasmagene which arises by mutation early in development. It multiplies faster than the cell, although not much faster in the early stages of development, and it is concentrated in the pollen grain, which is the slowest-growing cell in the plant.

This view is borne out by two additional pieces of evidence. Shoots sometimes occur which are patched with rogueness just as variegated plants are patched with colour (figure 3*c*), and in rogue-type crosses, when growth is hastened by the sterility of the flowers, the development of the full rogue character is deferred (Pellew, 1928).

Another important step in showing the part played in development by self-propagating particles in the cytoplasm has been taken by Spiegelman, working with yeast. Here it seems that important enzymes depend for their propagation both on nuclear genes, which provide their precursors, and on a substrate, which provides the materials fermented. This system gives us a credible account of the permanence of character of tissues in the higher animals.

The validity of such concepts is revealed by the circumstances of their occasional breakdown. It is a common observation that in piebald mammals—pigs or guinea-pigs—the black coloration of the skin covers a wider area than the black fur. Billingham and Medawar have made transplantation experiments to discover the cause of this spread of skin colour. They find that the black pigment is formed in cells in white areas which would not themselves normally form it. They are transformed as a result of infection from their black neighbours by a pigment determinant. This determinant must be a self-propagating protein, probably an enzyme, or a precursor of an enzyme, necessary for pigment production. Thus in an entirely neutral situation the basis of differentiation may be broken down by infection. The infection too is something new in being an internal infection. It is external only from the point of view of cell lineage and particle genetics.

CANCER

No less illuminating is the application of plasmagene theory, or particle genetics, to the development of tumours. In both plants and animals there are chemical agents, known as carcinogens, which change the properties of mature cells so as to make them resume growth and division. The new cell-lineage created by this mutation never returns to its normal character; it may change, but only by diverging further from that character. The production of proteins and nucleic acid is so enhanced that even the chromosome mechanism may break down: polyploid and fragmented

nuclei are formed like those arising under similar conditions in the red-cell precursors during pernicious anaemia.

The agents producing these changes most effectively are not the ones like the non-specific radiations known to yield ordinary gene mutations. They are chemical and specific. Moreover, some of them (e.g. aminoazobenzene) are even specific in their action on certain tissues. Now the cell nucleus is constant in nearly all tissues. Only the cytoplasm varies. Thus it seems to be the cytoplasm which reacts to the carcinogen. Cancer would thus owe its origin to a mutation in the self-propagating protein system of the cytoplasm, that is in a plasmagene.

The tumour thus represents a reversal of the normal government of the cell. In normal development the nucleus is in control. In the tumour the cytoplasm takes the bit between its teeth—with unhappy consequences. One of these consequences is that the new cell-lineage de-differentiates. Its enhanced rate of propagation, as a whole, is too great for some of its individual species of constituent. They are sorted out.

On this view also it now becomes possible to understand the different types of transmissibility in tumours. Some can be transplanted only by grafting, others can be injected by cell-free extracts, and others again are naturally infectious and therefore genuinely describable as viruses. In view of the fact that some plasmagenes are diffusible and others not, this variety of capacities in natural tumours is only what we should expect.

The field of immunology remains to be discussed. It is one of the most fruitful for the application of genetic principles. The directness of gene action in determining antigen production (especially with the Rhesus gene) is the basis of the finest genetic analysis so far carried out in man. The problems of immunology relating to cytoplasmic genetics are no less important but much more abstruse. It is enough at the moment to point out that if antibody production is regarded as a property of self-propagating cytoplasmic determinants it can be related to a growing body of verifiable hypotheses. For the utilization of this relationship, as proposed by Burnet and Fenner, the concepts of heredity, development, and cell infection have to be combined with an elasticity for which the present discussion may help to prepare us.

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Amedeo Avogadro

M. GIUA

Though Dalton succeeded—with difficulty—in winning general support for his theory of the atomic structure of matter, he himself was obsessed by the idea that all elementary atoms pursued a solitary existence. It is doubtful whether the conception of a congeries of atoms of the same element ever occurred to him. As a result, early formulation of chemical compounds was uncertain and often incorrect. It was left to Avogadro and, later, Cannizzaro to solve the problem, and so to clear the way for the rapid progress subsequently made in chemical theory.

Amedeo Avogadro of Quaregna and Cerreto, son of the magistrate Count Filippo and Anna Vercellone of Biella, was born in Turin on 9th August, 1776. Apparently the name Avogadro derives from 'De Advocatis,' a surname granted to church lawyers in recognition of special services. In 1789 he graduated in philosophy, in 1795 in law, and in the following year became Doctor of Canon Law. For some time he practised as a lawyer for the poor, but he soon devoted himself to mathematics and physics, and in 1803 handed his first paper to the Royal Academy of Sciences of Turin, of which he became a member. He began his teaching as mathematics and physics master at Vercelli Lyceum, and in 1820 he was appointed Professor of Higher Physics at Turin University. This chair, which had just been endowed, was suppressed after the 1821 revolution. After being restored in 1832 by King Charles Albert, it was held for some time by Cauchy and then offered again to Avogadro, who held it until 1850, when he was succeeded by his pupil Felice Chiò.

Amedeo Avogadro.

Avogadro was a man of a high humanistic as well as scientific culture and yet of great modesty. His ability earned him appointments as Member of the High Commission of Statistics, President of the Commission for Weights and Measures, and, after 1848, Member of the Higher Council for Education. His family life was uneventful. His wife, Felicita Mazzé of Biella, bore him six children.

It is not possible to appreciate fully the importance of Avogadro's work without considering also that of the great founder of the atomic theory, John Dalton. It is interesting to note that even in their personal characteristics the English and the Italian scientists were curiously alike. The history of science affords many examples of great builders of theories who were personally very modest, but in this happy characteristic Dalton and Avogadro are outstanding.

The work of Dalton led to the definition of relative atomic weights. By a similar approach, Avogadro introduced the idea of relative molecular weights. These two conceptions form the basis of the atomic-molecular theory with which the names of the two scientists are linked. The work of Dalton, as Stanislao Cannizzaro said, 'may be considered the most important step made by chemistry towards its perfection as a science.' Similarly, it may be justly said that Avogadro's work made Dalton's atomic theory of much greater use in chemistry, because he incorporated the atomic within the molecular theory, according to which aggregates of two or more atoms (i.e. molecules) exist, which chemical reactions may split into the constituent atoms.

The molecular theory was expounded by Avogadro in the classical paper '*Saggio di un modo di determinare le masse relative delle molecole elementari dei corpi e le proporzioni secondo le quali esse entrano in queste combinazioni*' (Essay on a Method of determining the Relative Masses of Elementary Molecules of Bodies and the Proportions in which they enter into Combination) [*J. Phys. Chim., d'Hist. Nat. et des Arts di De La Métherie*, **73**, 58 (1811)], and completed in numerous other papers, among which the following are worth mentioning: '*Sulle masse relative delle molecole nei corpi semplici*' (On Relative Masses of

Molecules in Simple Bodies) [*ibid.*, **78**, 131 (1814)]; '*Sul calore specifico dei gas composti paragonati con quello dei loro gas componenti*' (On the Specific Heat of Compound Gases as compared with that of their Gaseous Components) [*Giornale di Letteratura, Scienze ed Arti*, **4**, 478 (1816); **5**, 73 (1817)]; '*Nuove considerazioni sulla teoria delle proporzioni determinate nelle combinazioni e sulla determinazione delle masse delle molecole nei corpi*' (New Considerations on the Theory of Proportions determined in Combinations, and on the Determination of Molecular Masses in Bodies) [*Mem. Accad. Sci. Torino*, **26**, I (1821)]; '*Sulla necessità di distinguere le molecole integranti dei corpi dai loro equivalenti chimici nella determinazione dei loro volumi atomici*' (On the Necessity of distinguishing Molecules from their Chemical Equivalents in determining their Atomic Volume) [*Arch. sci. phys. et math.*, **8**, 285, (1849)]. Avogadro published a summary of his theory in the '*Trattato della costituzione generale dei corpi*' (Treatise on the General Constitution of Bodies) [Turin, 1838].

Dalton failed to realize the importance of Gay-Lussac's second law, but Avogadro saw the necessity of applying it to Dalton's theory, and says in his paper of 1811: 'Gay-Lussac showed that gases always combine in simple proportions by volume and that when the product of the reaction is a gas, its volume also bears a very simple ratio to that of the components; it seems that the ratios of the quantities of the elements cannot but depend on the relative number of molecules which combine, and on the number of resulting compound molecules. It is, therefore, obvious that very simple proportions exist between the volumes of the gaseous substances and the number of simple and compound molecules of which they are constituted. One is immediately led to the hypothesis which seems to be the only admissible one, viz. that equal volumes of gas contain the same number of molecules, and different volumes a proportional number of molecules.'

To understand Avogadro's reasoning, it must be remembered that by compound molecules he means the molecules in the modern sense, and by simple molecules he means what we call atoms. In modern form his well-known hypothesis reads: *Equal volumes of gases, at the same pressure and temperature, contain equal numbers of molecules.* This hypothesis gives us the means of determining the relative molecular masses of such substances as can be obtained in the gaseous state, and the relative number of molecules entering into combination. As the relations between the molecular masses are the same as between the densities of different gases, at the same pressure and temperature, the relative number of molecules combining is given by the relation of the volumes of the gases which combine. Thus the relative densities of oxygen and hydrogen, according to Avogadro's data, are respectively 1·10359 and 0·07321 (taking the density of atmospheric air as unity); hence the ratio of these two numbers represents the ratio of the masses of their molecules. Therefore the mass of the oxygen molecule is about fifteen times that of the hydrogen molecule, or, more accurately, the ratio is 15·074 : 1. Similarly the ratio of the mass of the nitrogen molecule to that of the hydrogen molecule is 0·9613 : 0·07321, or 13·238 : 1. On the other hand, as the ratio of the volume of hydrogen and the volume of oxygen which combine to form water is 2 : 1, it follows that water is formed by the union of one oxygen molecule with two hydrogen molecules. From this important statement, which is opposed to Dalton's assertion that one molecule of water contains one atom of oxygen and one of hydrogen, Avogadro drew the conclusion that molecules are divisible, contrary to the then current ideas of chemists and physicists. That the conception of the divisibility of the molecules was quite clear in his mind is evident from his discussion of the combination of two gases without change in volume. Consideration of Gay-Lussac's data on the combination of chlorine and hydrogen to form hydrogen chloride, and of nitrogen and oxygen to form nitric oxide, leads immediately, according to Avogadro, to the conclusion that the reacting molecules are split, as follows:

$$\underset{\text{chlorine}}{\text{1 vol.}} + \underset{\text{hydrogen}}{\text{1 vol.}} = \underset{\text{hydrogen chloride}}{\text{2 vol.}}$$

$$\underset{\text{nitrogen}}{\text{1 vol.}} + \underset{\text{oxygen}}{\text{1 vol.}} = \underset{\text{nitric oxide}}{\text{2 vol.}}$$

In other words, the molecules of chlorine, hydrogen, nitrogen, and oxygen must each have been halved, and must each therefore consist of an even number of atoms—at least two.

Avogadro concludes his paper with these words: 'The reader will have noticed that in many ways our results are similar to Dalton's, although we started from a general principle whereas Dalton bases his theory on particular considerations. This agreement supports our hypothesis which, in fact, is but Dalton's system enhanced in precision by the relation to Gay-Lussac's general principle which we have established. In Dalton's system, chemical reactions are generally supposed to take place in fixed proportions, and this has been confirmed by experiments, as far as the

more stable and interesting reactions are concerned. It seems that these are the only reactions which can take place between gaseous substances, because, if the ratio of the reacting gases were greater, the resulting molecules would become enormous in spite of the divisibility of the molecules, which in any case is probably restricted. It is easy to see that the closer contact between the molecules in solid and liquid substances, which makes the distance between compound molecules of the same order as that between elementary molecules, may lead to more complicated reaction or even to combination in any proportion whatever. But such reactions are, as it were, different from those with which we have dealt here, and this difference may perhaps help to reconcile Berthollet's theory of compounds with the theory of fixed proportions.'

Avogadro has been called 'the true legislator of the molecules' [I. Guareschi, 'Historical and Critical Considerations,' in the preface to Avogadro's selected works (*Opere Scelte*), 1911]. His contribution to the subject is indeed of a systematic and theoretical rather than experimental order. This may to some extent account for the delay in acceptance of his ideas, for, in spite of clear and repeated enunciation, his theory remained unheeded by chemists for thirty years. Graebe [*J. prakt. Chemie*, **87**, 145 (1913)] attributes this to lack of experimental support, but, even so, the tardy recognition of Avogadro's work is not easily explicable. His theory did, in fact, clarify many controversial points and, further, was not a mere statement of abstract or general speculations on the constitution of substances, but rested solidly on experimental results obtained by great chemists such as Gay-Lussac, Davy, and Berzelius. The assertion that chemists, particularly Berzelius, neglected Avogadro's papers because they were not published in chemical journals is no nearer the truth. It is more likely that workers in the first half of the nineteenth century were so engrossed in the experimental problems created by Lavoisier's antiphlogistic theory that they simply did not appreciate the value or realize the implications of Avogadro's work. The interpretation, in the light of Avogadro's hypothesis, of the experimental results of half a century of chemical investigations is due to Cannizzaro, whose '*Sunto di un corso de filosofia chimica*' (Summary of a Course of Chemical Philosophy) (1858) is the logical conclusion of Avogadro's work. Cannizzaro recognized this many years later: 'The corner-stone of modern atomic science is the theory put forward by Avogadro, Ampère, Krönig, and Clausius concerning the constitution of perfect gases, that is, that whatever their nature and their weight, they contain, in equal volumes and at the same temperature and pressure, the same number of molecules.' This is the logical starting-point for explaining the fundamental properties of molecules and atoms, and for establishing proof of the existence of the latter. Cannizzaro urges those who entertain any doubts on the subject to examine the mathematical basis of the evidence for the constitution of gases and to peruse the history of chemistry. This would convince them that, although Avogadro's and Ampère's theory seemed for a time at variance with physical facts, yet as the science of chemistry evolved and experimental data became co-ordinated, chemists gradually returned to their ideas. The work of Williamson, of Gerhardt, and of Frankland and Wurtz, explained most of the apparent exceptions to the law of equal volumes. Deville was able to explain the abnormal densities of some gases as being the densities of mixtures of dissociation products and not of single substances, and this explanation was confirmed by experiment. At the same time physicists were led to the same hypothesis—that equal volumes of gases contain the same number of molecules—from a new point of view. Cannizzaro ends his lengthy discussion with these enthusiastic words: 'Can there be any doubt that the convergence of scientific investigations on the same principle is the most decisive evidence in favour of the theory put forward by Avogadro and Ampère? To this theory scientists were led from different and even contrasting angles; it is a theory which forecast several facts which subsequent research has confirmed; it is a theory which must perforce be something more than a simple scientific abstraction. This theory must either be truth itself or the picture of truth as given by the instruments which interpret reality to our intelligence.'

The historian has to record the opinion of Nernst, viz. that the molecular theory and Avogadro's principle are the fundamental basis of chemistry.

Besides the main contribution on which his fame rests, Avogadro carried out many other investigations, which he published in four papers under the title: 'On Atomic Volumes of Elements and on Atomic Volumes of Solids and Liquids.' He also wrote some papers on electricity, which were read at the Academy of Sciences of Turin, the most important (1806) being on induction in non-conductors. He also constructed a voltmeter which was used in measuring certain electromagnetic phenomena.

Modern calculating machines

D. R. HARTREE

The idea of a large automatic calculating machine, flexible enough in operation to be used for a wide variety of calculations, was first conceived by Charles Babbage about 1835, but it was more than a century before his dream was translated into reality. Owing to financial and other difficulties Babbage's own machine was never completed, but modern calculators, using electronics in place of his purely mechanical devices, embody most of the fundamental ideas which he put forward. Calculating machines are now indispensable in science and industry.

It is convenient to distinguish between two main classes of equipment for carrying out numerical calculations by mechanical or electrical means. An example of one class is a device for carrying out the multiplication of two numbers x and y by passing a current, adjusted to have the value x amperes, through a resistance adjusted to have the value y ohms, and measuring the potential difference across the resistance in volts. In such a device the result is obtained by first representing the numbers by physical quantities of which they are the measures, then operating with these physical quantities (as, in this example, by passing the current through the resistance), and finally making a measurement of some physical quantity. Other examples of equipment of this class are the slide rule, planimeter, and most forms of harmonic analyser. A characteristic property of such devices is that their accuracy is determined by the accuracy of construction of the mechanical and electrical components of which they are built, and by the attainable accuracy of physical measurement.

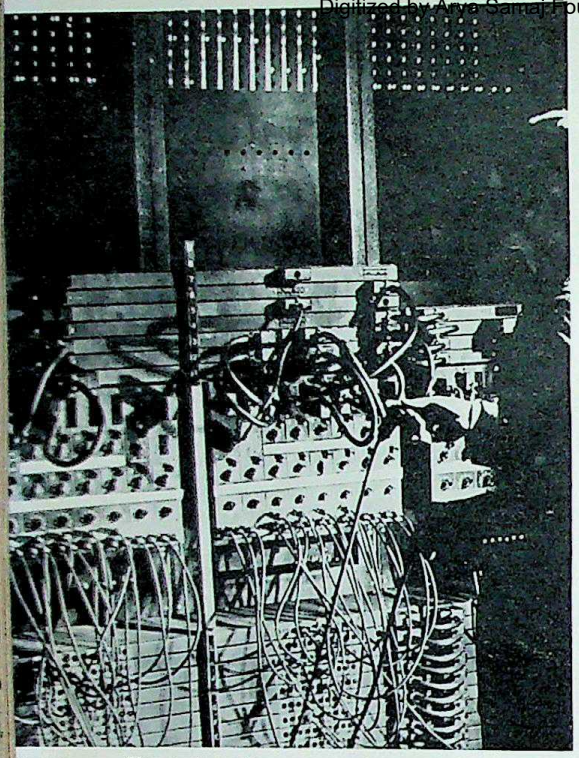
An example of the other class is the ordinary desk calculating machine such as the Brunsviga or Marchant. In a number written in the usual form, as 758, the symbols 7, 5, and 8 represent the digits of a number, and calculating devices of the second class operate directly with numbers expressed in this digital form, usually (but not necessarily) by counting either discrete objects, such as the teeth of a gear wheel (as in the Brunsviga), or discrete events, such as the reception of electrical pulses by an electrical counting circuit. Such devices cannot deal directly with continuously varying quantities. On the other hand, they can be built to work to any finite degree of accuracy; to get a result accurate to ten decimal places it is not necessary that any component of such a device should have an accuracy of 1 in 10^{10}.

Devices of the two classes are sometimes distinguished as analogous calculating 'instruments' and digital calculating 'machines' respectively, and it is with calculating machines, in this specialized sense, that this article is concerned. The main recent developments in this field have been in the direction of large machines capable of automatically carrying out extended sequences of computing operations, and so designed that the sequence of operations can readily be changed from that required for one calculation to that for another.

BABBAGE'S ANALYTICAL ENGINE

The idea of such a large, automatic, general-purpose machine is by no means new; it is over a hundred years old, though its practical realization is a development of the last ten years. The original conception of such a machine dates from about 1835 and is due to Charles Babbage, who at that time was Lucasian Professor of Mathematics in the University of Cambridge, and whose 'analytical engine' was to have been just such a machine [2, 3]. At that time, in the early days of the science of electricity, the 'analytical engine' was necessarily conceived as purely mechanical. But many of the functions required in the operation of such a machine can be carried out much more easily, and quickly, by the use of electrical components such as relays, uniselector switches, teleprinter equipment, and electronic valves, and such components are freely used in the machines recently completed or still in the course of development.

Babbage's machine was to consist of three main parts. One, which he called a 'store,' was to consist of a set of registers on which numerical information, either data of the problem or intermediate results, could be recorded in such a form as to be available for later use. Another, which he called the 'mill,' was to be able to carry out the operations of arithmetic on numbers transferred to it from the store. A third part, to which he did not give a name but which we may call the



URE 1 – *Front view of two accumulators of the electronic erical integrator and calculator (ENIAC).*

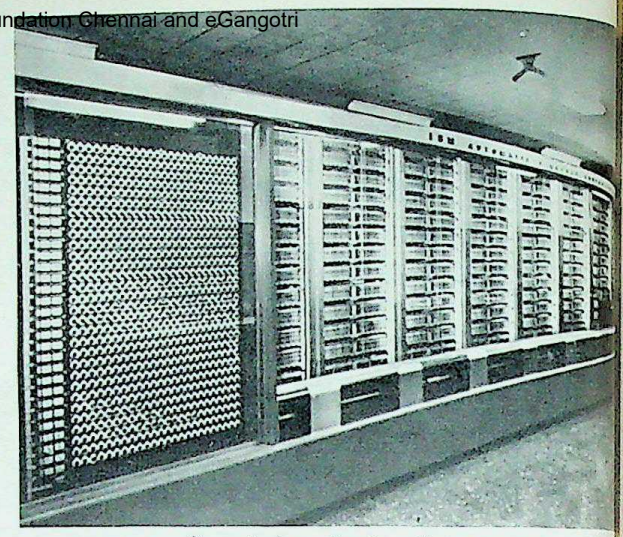


FIGURE 2 – *General view of automatic sequence-controlled*

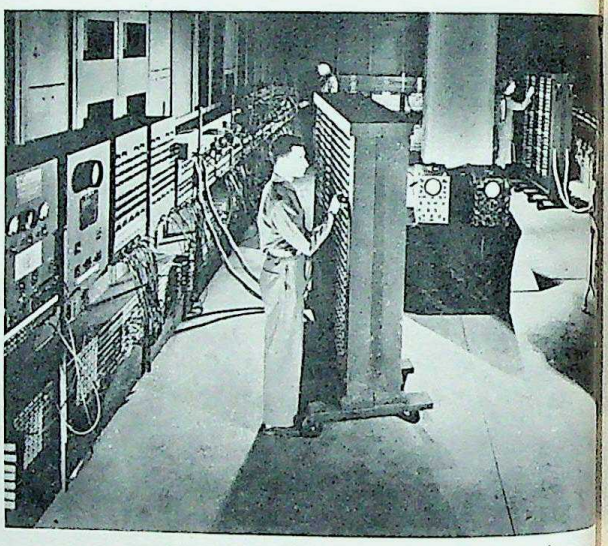
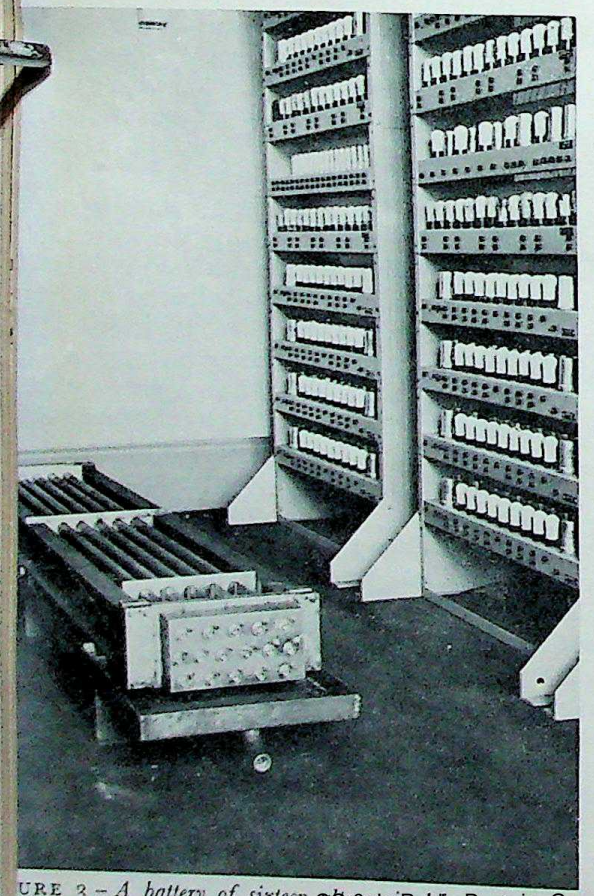


FIGURE 4 – *General view of the Eniac.*



URE 3 – *A battery of sixteen electronic relay units and associated equipment.*

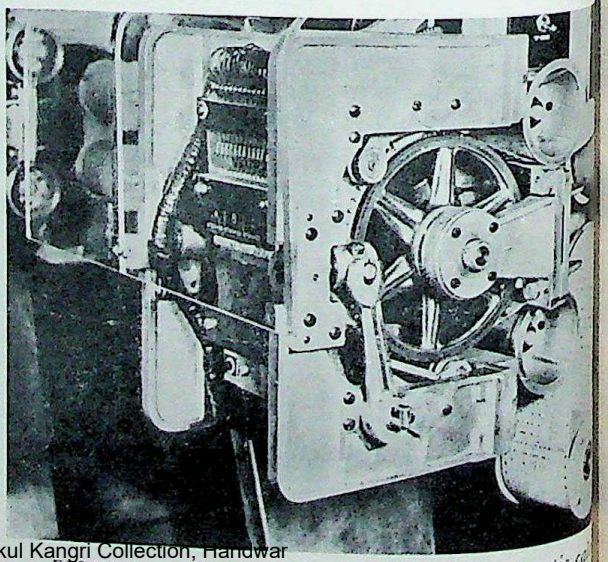


FIGURE 5 – *Sequence-control mechanism of automatic*

'controller,' was to take the operating instructions in the appropriate order and to control the operation of the machine in such a way that they were carried out. This control was to be exercised through a series of punched cards. Plungers passing through holes in the cards were to select the registers in the store from which numbers were to be transferred to the mill, the operation (addition, subtraction, multiplication, or division) to be carried out on them, and the disposal of the result.

FUNCTIONS TO BE PROVIDED IN AN AUTOMATIC CALCULATING MACHINE

This summary of the main features of Babbage's analytical engine illustrates the main functions to be provided in an automatic calculating machine. It must, of course, be able to carry out arithmetical operations, otherwise it would not be a calculating machine. This, however, is by no means all that is required. There must also be provided some form of storage, both for numbers and for instructions, and some form of control system for selecting numbers from the store and the operations to be carried out on them. It must also have some means of communication with the outside world, for reception of information, both numerical data and operating instructions, and for making a permanent record of the final results of its work.

Storage and control are aspects of such a machine at least as important as the means of carrying out arithmetical operations, and the scale and range of the calculations to which it can be applied depend greatly on the capacity of the store and the versatility of the control system. To give adequate flexibility without a human operator in the course of the calculation, the control system and the form of the operating instructions must be so planned that the sequence of operations carried out by the machine can be modified automatically by the results of the calculation as it proceeds. This is usually done as follows. Any one instruction must not only specify an operation to be performed but must determine in some way the next instruction to be taken. Control of the sequence of operations by the results of the calculation is effected by making the selection of the next instruction, at certain stages of the work, depend on some criterion, such as the sign of some number evaluated in the course of it. Over a hundred years ago Babbage recognized the importance of this process of conditional selection of the next instruction in the organization of any extensive calculation, and devised means of carrying it out mechanically; it is surprising that several recent accounts of the 'analytical engine' make no reference to this feature.

'BABBAGE'S DREAM COME TRUE'

The first such machine to be built was the I.B.M. Automatic Sequence-controlled Calculator (known for short as the Harvard Mark I Calculator) developed by Professor H. H. Aiken and the I.B.M. Company and now installed at the Computation Laboratory at Harvard University [1, 4, 13]. This machine was completed during the recent war. In its physical form, with its extensive use of electrical components, it is very different from anything Babbage could have envisaged. But in what it does, as distinct from how it does it, it is in many respects similar in principle to Babbage's 'analytical engine,' and it has been hailed as 'Babbage's dream come true' [8].

In this machine arithmetical operations are carried out by mechanical counters operated through electromagnetic clutches controlled by relays; 72 of these counters combine the functions of storage units and adding units, others form parts of units for carrying out multiplication, division, interpolation, and other functions. The machine has built into it means of evaluating logarithms and antilogarithms to base 10 and sines; other tabular information can be supplied from punched tape. The control of operations is also carried out by a tape, on which instructions are punched in coded form. Contacts made through the holes in this tape close circuits which actuate relays, and these close other circuits which cause the operation specified by the coded instruction to be carried out. Results can be delivered either on punched cards or by means of automatic electric typewriters.

A front view of this machine from the left-hand end is shown in figure 2. On the left are switches for setting values of constants or initial data by hand, then banks of counters, and then the interpolator and sequence control units; the controlling relays are mounted on panels at the back. Figure 5 shows a close-up view of the sequence-control unit with a tape in position.

In this machine relays are used purely for control. In some other machines, including one large general-purpose machine built by the Bell Telephone Laboratories [26] and another (the Harvard Mark II Calculator) by Professor Aiken [7], relays are used for arithmetical and storage purposes also, numbers being represented by the configurations of groups of relays. Addition is carried out, not by counting (which consists of successive addition of units), but by means of an

addition table built into the machine by connections between three groups of relays of the arithmetical unit, one group for each of the two addends and one for the result. As in the Harvard Mark I machine, the sequence of operations is supplied to the machine in coded form on punched tape.

Another machine is the Eniac (Electronic Numerical Integrator and Calculator) developed by Dr J. P. Eckert and Dr J. W. Mauchly at the University of Pennsylvania [6, 10, 11, 18, 19]. This is the first machine to be built which makes use of electronic circuits rather than electromechanical components; it is correspondingly faster than the others mentioned. It carries out an addition in 0·2 millisecond and a multiplication in less than 3 milliseconds, that is, at the rate of about a million multiplications an hour. It operates by counting electrical pulses produced by a pulse generator and switched to the different units of the machine by electronic gate circuits, the counting being done by electronic counting circuits. These counting circuits are grouped into twenty registers ('accumulators'), each of which serves both as an adding unit and as a storage unit. Tabular information required in the calculation is set up by hand on banks of switches, and numerical data can also be supplied from punched cards. The sequence of operations is specified by the interconnections between the various units of the machine and the settings of various control switches; these interconnections and switch settings are made manually in setting up the machine for any particular problem. Figure 4 shows a general view of this machine, and figure 1 is a close-up view of the front of two accumulators, showing the plug-in connections and switches by which the sequence of operations is furnished to the machine.

Another machine, combining the features of electronic circuits for carrying out arithmetical operations, as in the Eniac, and the use of a punched control tape for setting up the interconnections between the different units of the machine automatically as they are wanted, as in the Harvard Mark I Calculator, was completed by the I.B.M. Company early in 1948. This is a very large machine, comprising about 15,000 electronic valves and a similar number of relays, and can be regarded as the culmination of the first stage in the development of automatic calculating machines. The next stage, represented by machines still under development (one or two may be completed by the time this article appears) promises to provide machines which will be faster, having greater storage capacity with rapid access; will be at least as versatile and yet comprise a much smaller number of electrical components; and for which the "programming" of a calculation will probably be easier.

THE MAIN DIRECTIONS OF CURRENT DEVELOPMENT

This next stage is marked by two main features. One is the development of a reliable form of storage system which will give a large storage capacity with rapid access and without a large amount of electronic equipment. The other is concerned with the form of the instructions and how they are stored and used in the machine.

There are at present three physical forms of storage which appear to have been developed far enough to be of use for this purpose in the near future. These are (*a*) acoustic delay lines, in which the data to be stored are represented by trains of pulses (possibly on a carrier) [17, 20]; (*b*) magnetic material, on which the data are represented by variations in the magnetic state of the material; and (*c*) an electrostatic charge distribution on an insulating screen [9, 15, 25].

The usual form of acoustic delay line is shown diagrammatically in figure 6. A tube fitted with a piezo-electric quartz crystal at each end is filled with mercury. Electrical pulses applied at the transmitting end (left-hand end in figure 6) are converted into acoustic pulses in the mercury, travel down the tube, and are reconverted into electrical pulses at the other end. These are amplified and used to gate pulses from a pulse generator ('clock') to the transmitting end of the delay line, thus avoiding any progressive degeneration in the pulse shape. Gating of clock pulses is also used to ensure synchronism between the operation of different parts of the machine. With a pulse spacing of 1 microsecond a storage capacity for 1,000 numbers, each of ten decimal digits, can be provided by thirty such tubes, each 150 cm long.

Several machines using this form of storage are

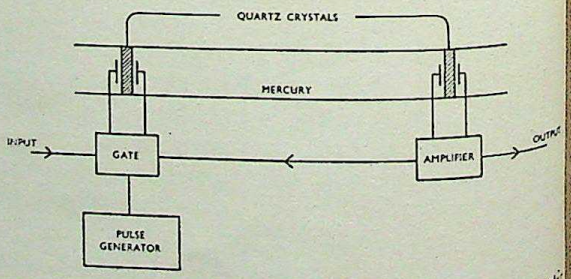


FIGURE 6 – *Diagram illustrating the use of an acoustic delay line as a storage unit.*

under construction at present. They include the 'Edvac' (Electronic Discrete Variable Automatic Computer) at the University of Pennsylvania and the 'Univac' being built by Eckert and Mauchly, the designers of the Eniac, and others in the United States, and in England the 'Edsac' at the Mathematical Laboratory at the University of Cambridge [21] and the A.C.E. (Automatic Computing Engine) at the National Physical Laboratory [22]. Figure 3 shows a battery of storage delay lines and panels of valves and other elements of the associated circuits of the 'Edsac.'

Magnetic material in the form of a wire or tape is used as an auxiliary storage medium in several machines. In the form of a coating on a cylinder which is rotated at high speed ('magnetic drum') it is used as the main storage in two machines. One of these is the Harvard Mark III Calculator which is being built by Professor Aiken; in this machine arithmetical operations are carried out by electronic circuits. The other is the A.R.C. (Automatic Relay Computer) being built by Dr A. D. Booth at the Research Laboratories of the British Rubber Producers' Association [5], in which they are carried out by relay circuits.

A form of electrostatic storage using a standard cathode-ray tube has been developed by Professor F. C. Williams of Manchester University [24, 25], and a simple experimental machine using this storage system has been operated satisfactorily [23]. In the United States work is in progress on the development of special tubes for electrostatic storage [9, 15]. In a machine under construction at Princeton it is intended to use a group of such tubes for the primary storage, with electronic computing circuits and magnetic wire for auxiliary storage.

In most of these machines there is no distinction between the forms in which numbers and instructions are represented in the machine; both, in most cases, consist of a series of indications (such as presence or absence of pulses) which can be interpreted numerically as 1's and 0's. The difference, if any, between numbers and instructions is in the way they are used. This has two consequences; firstly, the same storage system can be used for numbers and for instructions, and secondly, arithmetical and other operations can be carried out on the instructions. This possibility of modifying the instructions in the course of a calculation may considerably reduce the storage space required for instructions, and, combined with the operation of conditional selection of the next instruction, makes such a machine very flexible and applicable to work involving a high degree of discrimination.

Figures 1 and 4 are reproduced by courtesy of the U.S. War Department; figures 2 and 5 by courtesy of the Harvard University Computation Laboratory; figure 3 by courtesy of Dr M. V. Wilkes.

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Draughtsmanship in zoological work

GEOFFREY LAPAGE

The purpose of scientific drawings is essentially utilitarian, namely to record in graphic form certain attributes of the objects depicted, those attributes being such as the scientist regards as significant. Scientific art thus differs from pure art, and any aesthetic appeal that scientific drawings may happen to possess is secondary, though not always fortuitous. Dr Lapage describes some masterpieces of scientific draughtmanship, with illustrations.

This article considers some drawings made by men of science. These drawings were made for the primary purpose of stating, in pictorial form, certain facts which had been scientifically observed, and it is thus possible, theoretically at least, to consider them as being fundamentally different from an artistic drawing. The nature of that difference, and the question whether a man of science, or any other human being for that matter, can eliminate art entirely from his drawing, cannot be discussed here. Such a discussion would involve an analysis of what it is that the scientist and the artist respectively aim to do, and this would take us beyond the limits of the present article.

The few drawings here reproduced cannot, of course, be representative of the many that deserve our admiration. They must be considered merely as one man's more or less arbitrary selection; other people could no doubt quite easily select a different series which would be just as suitable for the purposes of this article, as indeed the writer himself could. So numerous are the available fine examples of the draughtsmanship of men of science that it has been necessary to impose severe restrictions upon the selection. The choice has been restricted, first, to drawings made by men of science no longer living; and, second, to those which illustrate one branch of science only. The branch of science chosen is the study of the structure and architecture of animals, and drawings of a number of different kinds of animals have been purposely selected.

The name that springs naturally to the mind when drawings of the structure of living things are discussed is that of Leonardo da Vinci (1452–1519). Originally, a drawing by this master was included in the series of illustrations, but it was omitted, first, because Leonardo's drawings of plant and animal structure are very well known and, second, because no single Leonardo drawing in this category could illustrate adequately the variety of techniques that he employed, or the whole of his mastery. Leonardo's drawings, moreover, inevitably raise acutely the problem mentioned in the first paragraph, for the discussion of which we have not space. The influence of his work is so compelling, and the two motives of science and art were so closely interwoven in him that it is always difficult to decide whether, when he made a drawing of the structure of an animal or plant, he was behaving purely as a scientist or not.

This same problem is, of course, latent in many scientific drawings. It rears its head unmistakably for instance, in the fine copperplate engraving of a carp illustrated in figure 8. This drawing, done at some time between 1554 and 1558, is the work of Leonardo's countryman Hippolyto Salviani, who was a physician in Rome. The beautiful quality of the line, the management of the light and shade, the delicate balance of the whole drawing, and the life and beauty communicated to it are indeed remarkable. A glance through the volume [1] from which this drawing has been reproduced will show that Salviani, whatever his achievements as a medical man, had much of the artist in him to contend with his scientific interests and also that he was a master of this particular technique.

Another remarkable drawing by an Italian contemporary of Salviani, the Bolognan Senator Carlo Ruini (1530–98), is the drawing of a horse's head reproduced in figure 5. This example of a different line technique is justly famous among students of comparative anatomy. Apart from its historical and scientific value it has a fine decorative quality which has nothing to do with science. It has been reproduced from Professor F. J. Cole's fascinating book [2] on the history of comparative anatomy, a volume which contains many illustrations that will interest and delight students of this subject.

FIGURE 2 – *Illustration of an insect* (Proctotrupes areolator), *painted by John Curtis for his* British Entomology (1839).

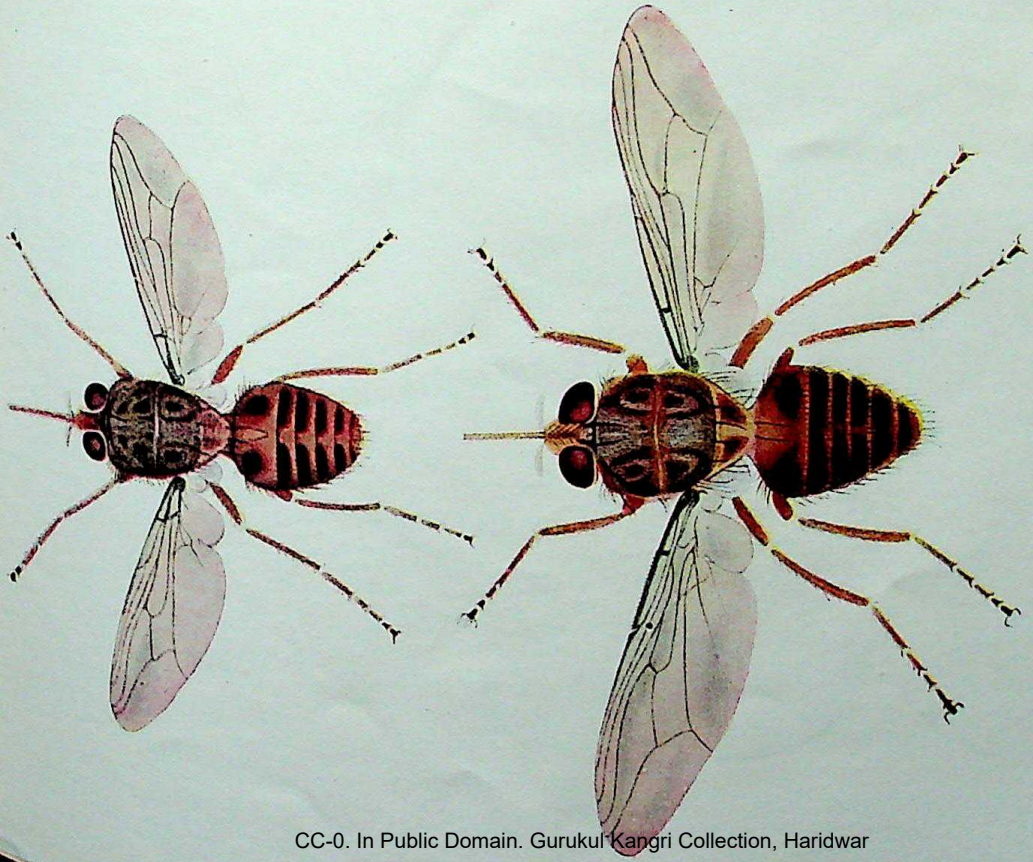


FIGURE 1 – *Painting of tsetse flies, by the late Professor R. Newstead* (1924).

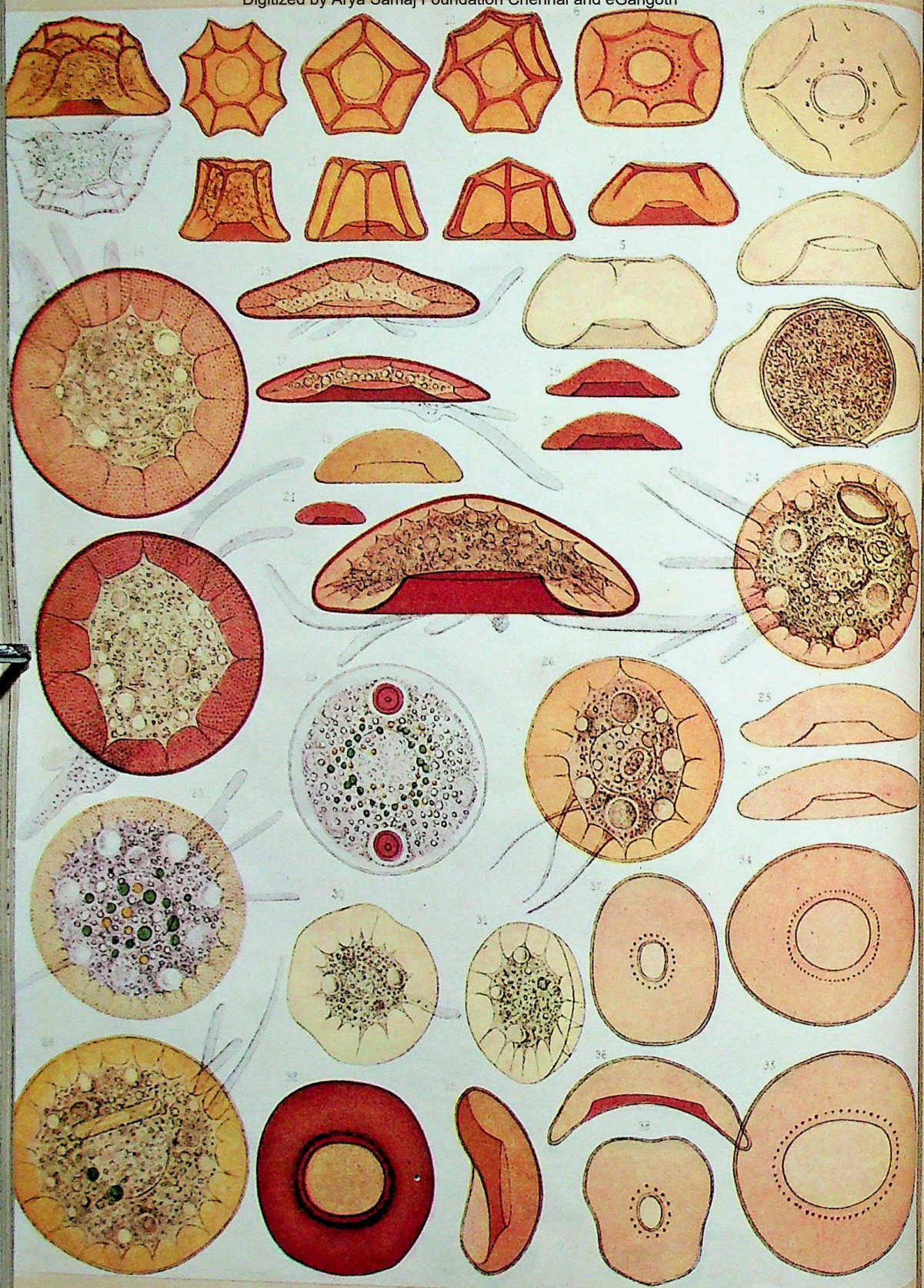


FIGURE 3 – *Illustrations drawn by J. Leidy for his* Report of the United States Geological Survey of the Territories (1878)

Turning now to another technique, the art of engraving upon wood, we advance a couple of centuries to the example, shown in figure 4, of the work of a man who was not only a naturalist and a student of humanity but also a great master of this difficult technique. The wood engravings of Thomas Bewick (1753–1828) are so justly famous that they need no comment here. This drawing of a tawny owl, which is one of the numerous and remarkable illustrations in his *History of British Birds* [3], well shows one feature of his work upon which his fame rests, namely his revival of the use, in wood engravings, of white spaces and lines. His work also owes something to the contemporary introduction of boxwood cut across the grain for work of this kind.

Wood-block engraving, capable though it is—in the hands of those who have mastered it—of producing results so clear and telling and beautiful, is not a technique that a busy man of science, bent primarily upon stating certain facts in pictorial form, would naturally use. Like etching, engraving upon metal, and drawing direct upon the lithographic stone, it demands a degree of technical skill and a love of the craft which are more likely to be found in the artist than in the scientist. All these techniques have, however, been used by men of science, although frequently it is difficult to ascertain whether the men of science who used them actually engraved the wood or metal or drew upon the lithographic stone. Often they made drawings which were engraved or lithographed by professional engravers or lithographers, so that many scientific drawings reproduced by these techniques are copies of the drawings made by the men of science. Some scientists have gratefully acknowledged the work of the engravers or lithographers who thus copied their drawings. A. D. Michael, for instance, tells us that the beautiful illustrations to his Ray Society monographs on oribatid mites were drawn for him upon the lithographic stone by the lithographers Rhein and Knight, whose skill and care he gratefully acknowledges. Ernst Haeckel, whose drawings of the remarkable microscopic skeletons of the marine radiolaria are so deservedly famous, tells us of his gratitude and debt to his lithographer, Adolph Giltsch, who co-operated with him for ten years on this particular work; but Haeckel provides us in this great monograph, and in his works on the medusae and other coelenterates, and also in his *Kunstformen in der Natur*, with evidence that he himself was a remarkable draughtsman.

Others who have had to rely upon professional

FIGURE 4 – *Tawny Owl: a woodcut by T. Bewick for his* History of British Birds.

engravers or lithographers have rightly been disappointed by the printed results. P. H. Gosse, for instance, whose work is further discussed below, took endless trouble over the illustrations to his books and himself drew some of them upon the lithographic stone; but the poor quality of the colour in the illustrations that were actually published caused him to take exceptional care with the illustrations for his book *The Aquarium*, published in 1854. These, says his distinguished son, Sir Edmund Gosse [5], achieved an 'unprecedented beauty' and 'marked an epoch in the annals of British book illustration.'

Another devoted worker who was not satisfied with the colour lithographs of the drawings that he had made was the American, Joseph Leidy, an example of whose work is reproduced in figure 3. This illustration shows some of the many beautiful drawings in colour and in black-and-white which Leidy made to illustrate his great work [6] on the freshwater rhizopoda of North America.

Two other lithographs, reproduced in figures 9 and 10, illustrate the results that can be obtained by this technique when colour is not employed. The first one (figure 9) is reproduced from the well-known monograph on ticks and mites by the French expert, P. Mégnin [7], and shows very well the delicacy and clarity of the effects that can be obtained by this method. The second one (figure 10) is by the English zoologist Herbert Fowler [8]. It shows how a lithograph

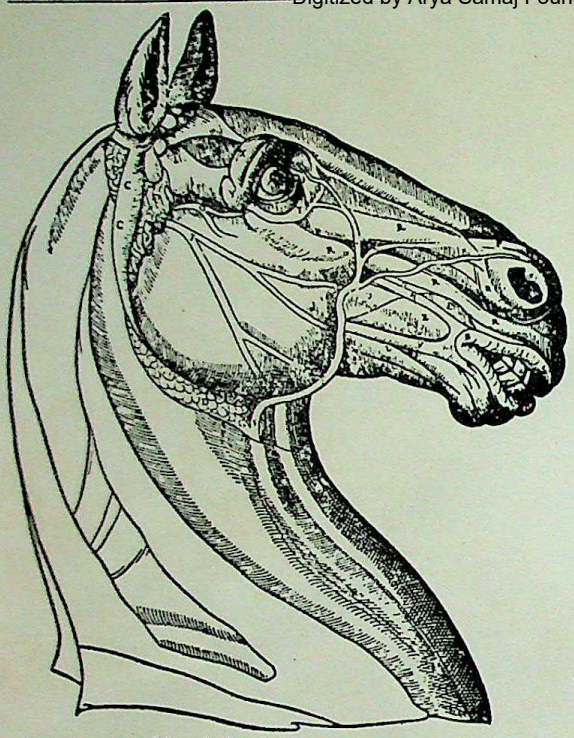


FIGURE 5 – *Horse's head, showing muscles, vessels, nerves, and glands, drawn by C. Ruini* (1598).
(*From* History of Comparative Anatomy *by Prof. F. J. Cole, published by Macmillan & Co. Ltd.*)

may be used not only to state scientific facts but to interpret them to the student as well.

Also designed to interpret the structure of animals, as well as to state the facts of that structure, are the drawings illustrated in figures 7 and 11. All these are examples of a kind of drawing the purpose of which may be called instructional. They do not state all the scientific structural facts: they select only some of them, and emphasize them in such a way that the student may at a glance get an accurate three-dimensional picture of the architecture of the animals depicted. Figure 7, which omits the colour used in the original, is one of the many drawings of this kind which illustrate the well-known textbook of zoology by Yves Delage and Edgard Hérouard [9]. This particular drawing explains the structure of an organism of the jelly-fish type, *Porpita*.

Figure 11, by Sir Edwin Ray Lankester [10], achieves, by the use of line only, or by line with the addition of stipple here and there, the same interpretative and instructional result. There are many drawings similar to these, most of them relatively modern, which contain not only the descriptive element which all scientific drawings have, but a creative element also, supplied by the knowledge and experience of the man of science who makes the drawing. In this sense they are personal, like the drawings of all artists, but their personal quality is not, like that of the artist's drawings, emotional; it is intellectual. The human quality of the scientist does not appear in his drawing; only his interpretative brain is apparent. He has, so to speak, projected his experience into the object portrayed, and has, by that act, created an imaginative conception which embodies contemporary scientific knowledge of the object.

Other drawings of this kind which will occur to biological readers are E. S. Goodrich's drawings illustrating his well-known work on the renal excretory organs and other structural features of vertebrates; Ray Lankester's diagram of an ancestral mollusc, which embodies the primitive structural features from which the anatomical characteristics of all the shellfish can be derived; the stereograms used by J. S. Kingsley and others to depict the architecture of backboned animals; and the illustrations in Sir D'Arcy Thompson's classical work, *Growth and Form*.

There remain for comment the three drawings in colour by R. Newstead (figure 1), John Curtis (figure 2), and P. H. Gosse (figure 6). The water-colour by P. H. Gosse, which has never been published before, is reproduced here from the original painting in the possession of Dr Philip Gosse, who courteously and very willingly gave permission to reproduce it. It has been chosen from a number of other original and unpublished paintings by P. H. Gosse which the writer has been privileged to see. The delicacy of all these paintings, the certainty of touch that they show, their accuracy, and the beautiful quality of their technique indicate clearly that P. H. Gosse brought considerable artistic ability to the scientific study of animals. No doubt he inherited this from his father, who was a miniaturist, and perhaps he learned from his father his skill in copying exactly the fine shades of colour and details of structure of the animals which he studied. Sir Edmund Gosse [5] has said that his father's interest in natural subjects was chiefly 'aesthetic and poetical, depending upon the beauty and ingenuity of the forms.' Certainly his eagerness to make accurate and beautiful drawings of the animals which he collected was remarkable.

Gosse was, of course, one of a company of naturalists whose black-and-white and coloured illustrations of their works excite the admiration of anyone interested in draughtsmanship. Some of these men live on in the beautiful drawings which are among the treasures of our libraries;

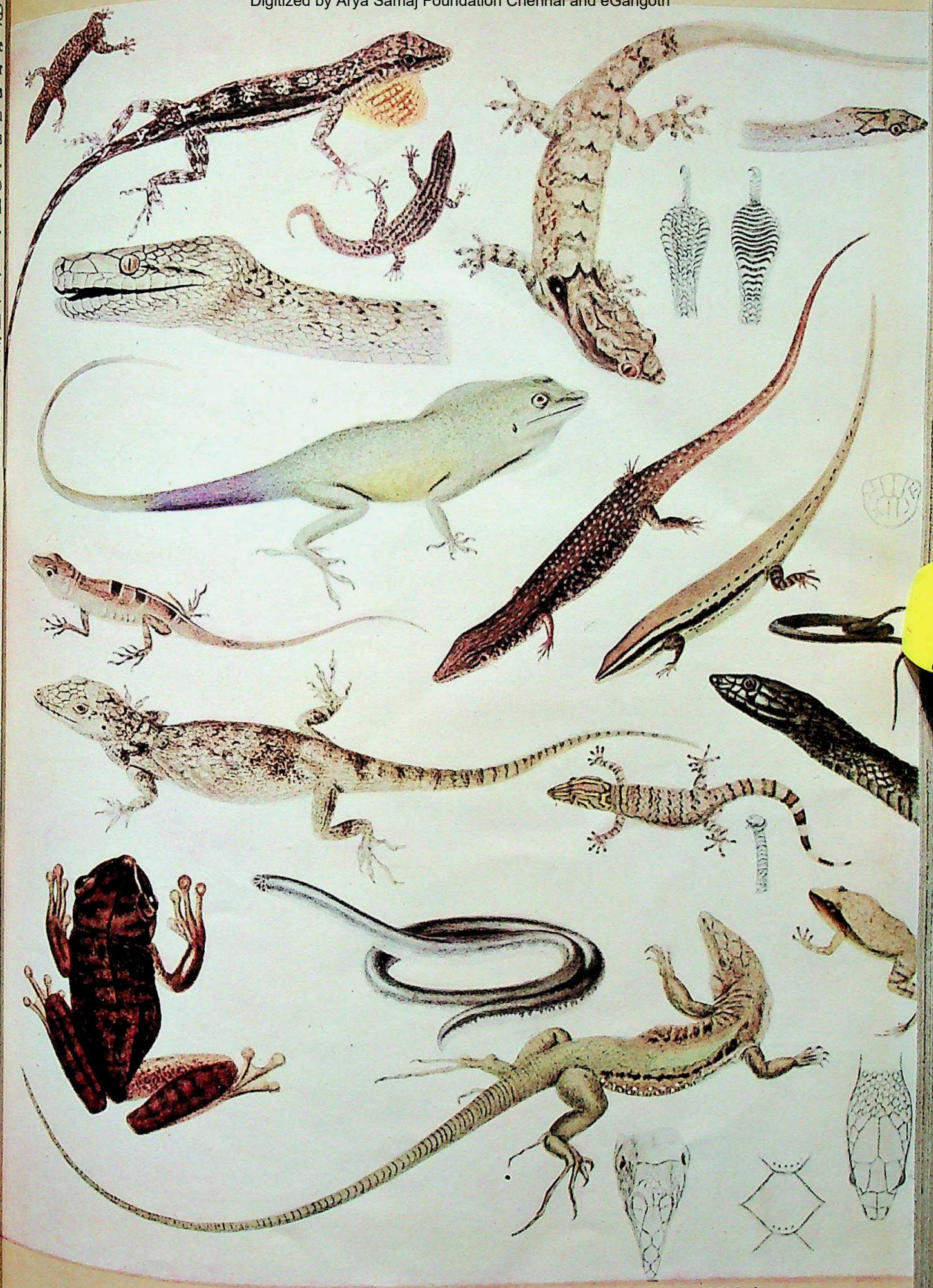


FIGURE 6 – *A water-colour painted by P. H. Gosse and never previously published.*

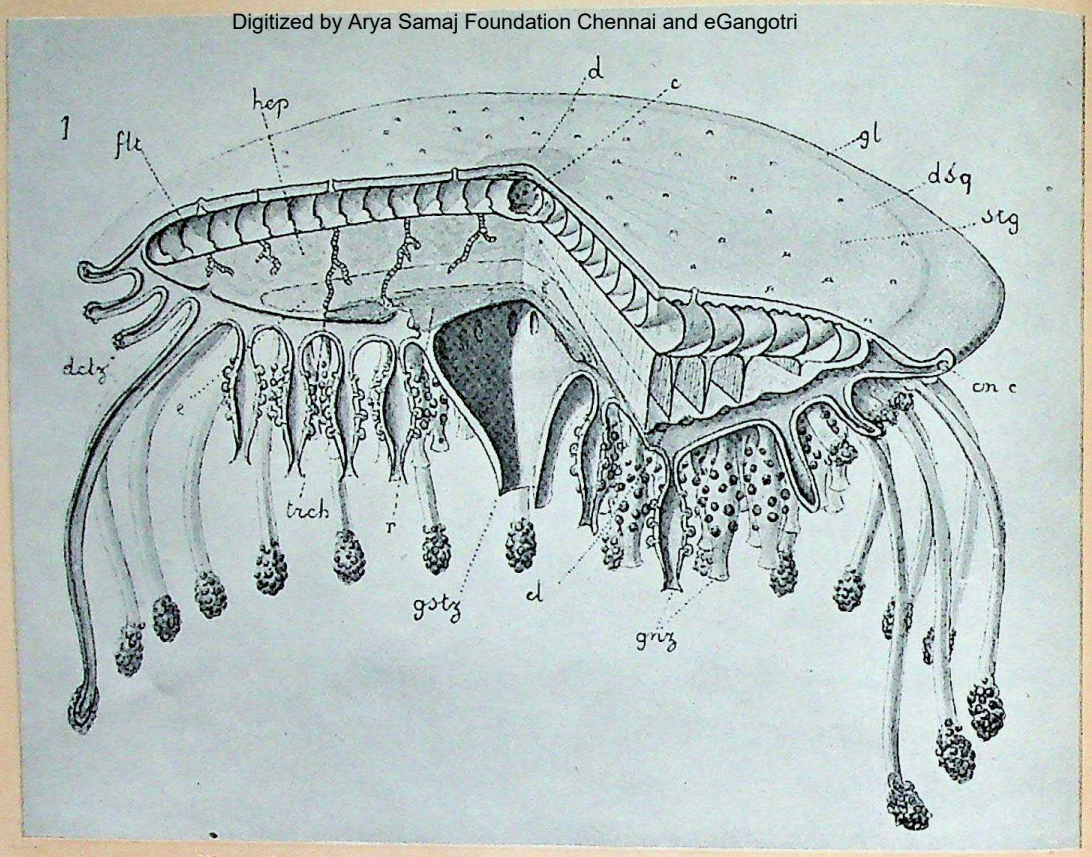


FIGURE 7 – *Illustration of jelly-fish* (Porpita) *from the coloured illustration in* Traité de Zoologie Concrète, *by Y. Delage and E. Hérouard* (1901).

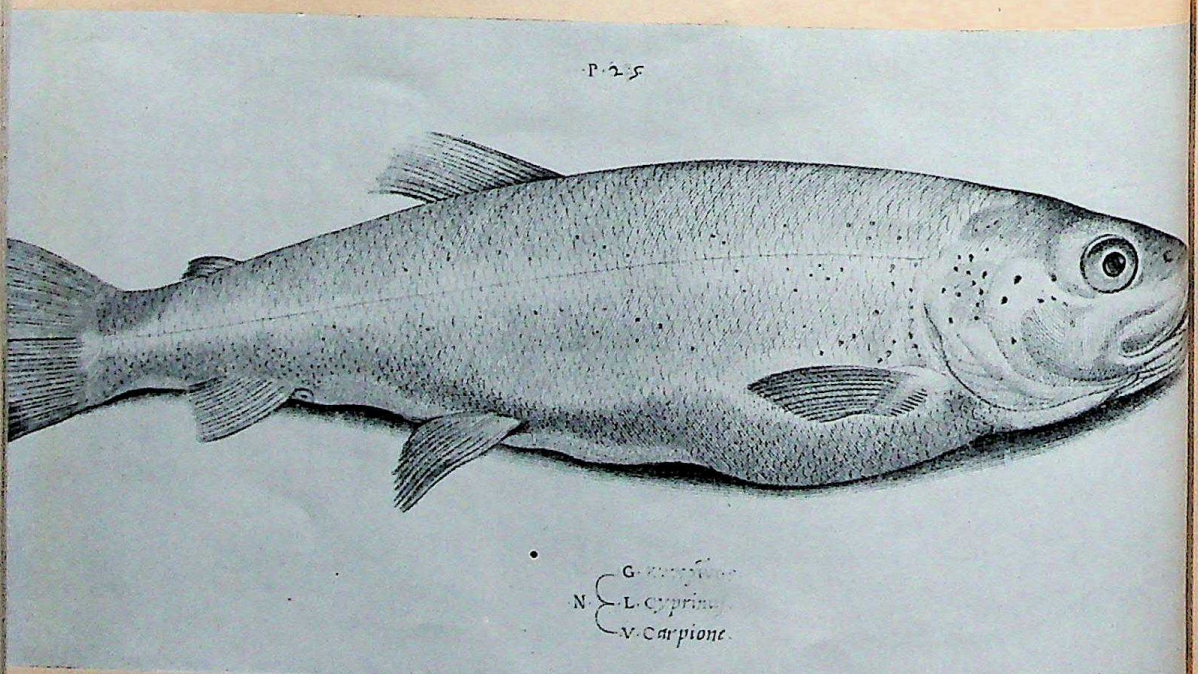


FIGURE 8 – *Copperplate engraving of a carp, made about* 1556 *by Hippolyto Salviani.*

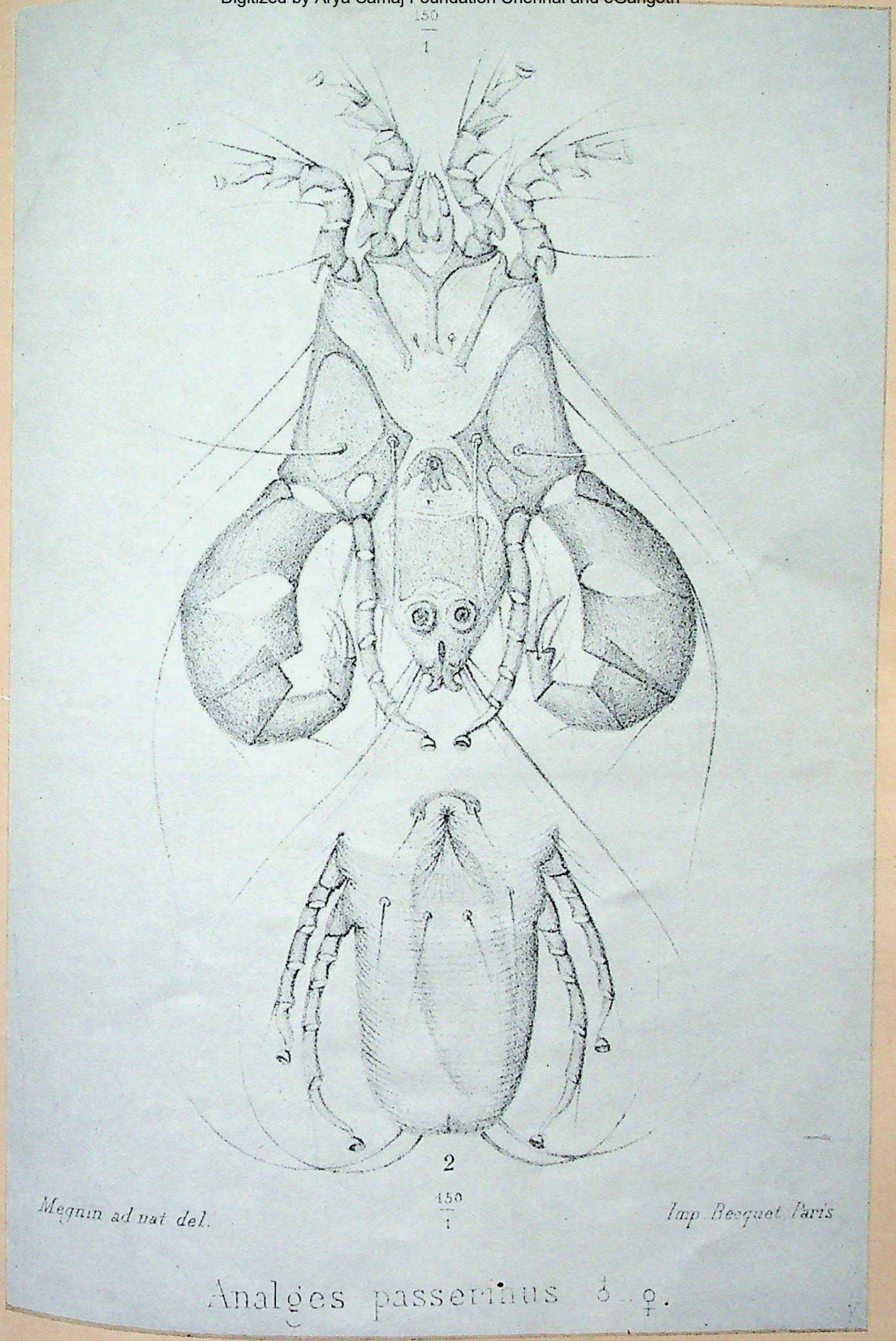
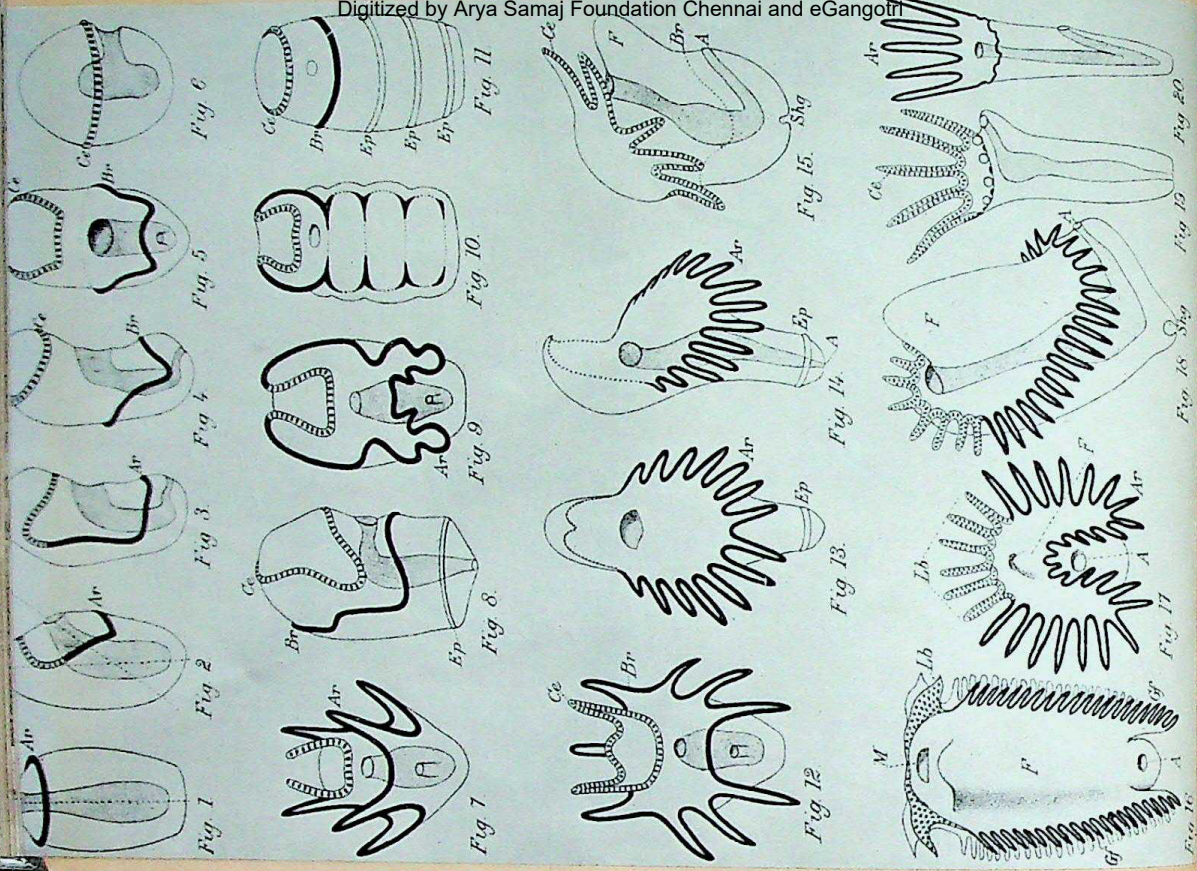
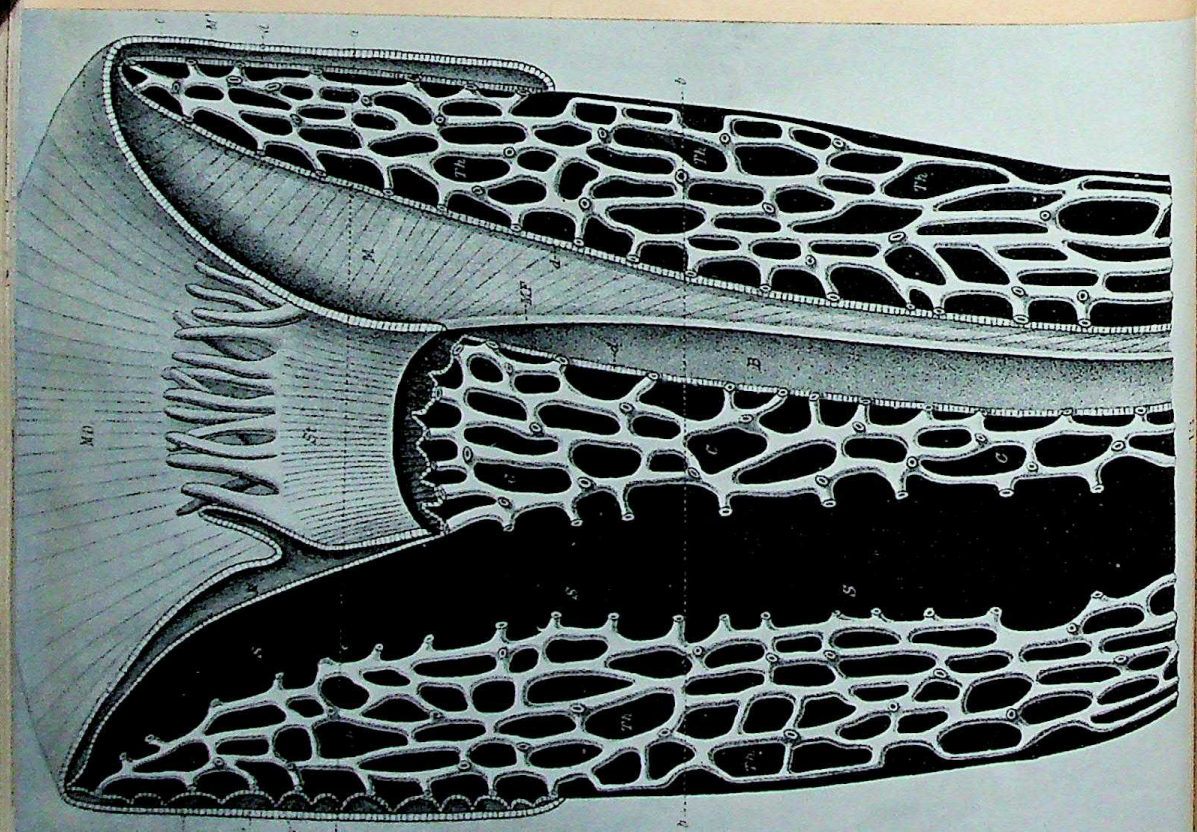


FIGURE 9 – *Lithograph of a tick* (Analges passerinus), *by P. Mégnin* (1895).





others, like our great orators and actors, live only in the tributes of those who came under their influence. Such a man was Gosse's contemporary, the Rev. J. G. Wood, who carried with him on his extensive lecturing tours a canvas supported on an iron frame, on which he illustrated with coloured chalks his very successful lectures on natural history. There have also been, as all of us know well, countless lecturers in our universities, whose extemporary drawings on the blackboard have not only instructed but have delighted and astonished those who saw and profited by them. To mention any of these by name would be to leave many of their fellows in undeserved oblivion.

The two other paintings which complete the small series here illustrated are both by entomologists. John Curtis, whose work is illustrated by figure 2, was a naturalist who, like Gosse, gave his life to his work. The delicate and beautiful drawing is taken from the last (16th) volume of this author's well-known work *British Entomology* [11]. It is chosen from this volume because Curtis says in his preface to the whole work that the plates which illustrate this last volume are by himself. Some of the illustrations in the other volumes were, he says, done by artists whom he called on to help him to complete this considerable treatise —which is, incidentally, an outstanding example of the former but now rare practice of obtaining pre-publication subscriptions to cover the cost of a work which might bring little financial reward to the author. The prolonged labour, the loving care, and the high degree of technical achievement displayed by this and other publications issued in the same manner are features of the scientific life of earlier days. Nowadays, in an age of hurry, there is too often preference for the photograph, and an inclination to leave the illustration of scientific work to professional illustrators.

Here and there, however, the old tradition lives on, as the painting of tsetse flies (figure 1) by the late Professor Newstead [12] of the Liverpool School of Tropical Medicine manifests. This shows that Newstead, whose reputation among biologists as a draughtsman was world-wide and deeply respected, was very well qualified to keep alive that devotion to the proper illustration of biological work which always has been, and still is, the mark of the master of this branch of science. His work is a worthy link between the fine examples of scientific draughtsmanship left to us by his predecessors and the beautiful drawings which living biologists, who eagerly take advantage of the advances made by the printer in methods of reproduction, are nowadays producing so abundantly.

ACKNOWLEDGMENTS

The photographs which illustrate this article were taken in the Zoology Department, University of Cambridge, and the writer is greatly indebted to Professor Gray for permission to use the excellent technical facilities available in that department, and also for permission to use the Balfour Library. He is also grateful to those members of Professor Gray's technical staff who gave their assistance, and to the librarian of the Balfour Library and others whom he consulted about the selection of the illustrations. He gratefully acknowledges the permission given by the Company of Biologists Limited to use the drawings reproduced in figures 10 and 11.

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Foetal haemoglobin

J. C. KENDREW

Because of its practical importance and its intrinsic interest the problem of foetal circulation has been very closely studied. Recent research has established not only that—contrary to popular belief—the maternal and foetal blood never mix, but that the haemoglobins in the two blood-systems possess small but important differences. The latter are reflected in their oxygen dissociation curves, in the speed of alkaline denaturation, and in other ways, though the physiological and structural significance of these differences is not yet clear.

The popular mind still harbours the superstition that a mother's blood circulates through the arteries and veins of her unborn child—a superstition doubtless connected with the myth that our hereditary characteristics are derived from the blood, blue or otherwise, which has been transmitted to us from generation to generation. In point of fact the foetal circulation is quite distinct and separate from the maternal at all stages of development. The two bloods never mix, though indeed they come into close proximity in the placenta, an organ whose prime function is to ensure that the maternal and foetal circulations are placed in so intimate a relation that the food and other materials required by the foetus can diffuse from the former into the latter, and the metabolic waste products in the contrary direction. In the placenta the capillary vessels of the two circulatory systems are separated, but only by a membrane whose thickness may vary from one layer of cells (in the rabbit) up to five or six layers (in the ruminants). In this article we shall be concerned with the supply of the most essential of all substances required by the foetus, namely oxygen.

The haemoglobin of red corpuscles is, of course, the oxygen-carrier of blood, and its reversible combination with oxygen is illustrated in figure 8 (A), which shows that at high oxygen pressures (e.g. in the lungs) the haemoglobin is largely oxygenated, while at low oxygen pressures (e.g. in the tissue capillaries) it gives up most of its oxygen for transfer to the cellular oxidation-reduction systems. If the maternal and foetal bloods had the same oxygen dissociation curves it is clear that oxygen would be transferred in the required direction, since the oxygenated arterial blood of the mother would lose oxygen to the deoxygenated venous blood of the foetus, an oxygen pressure-gradient being set up across the placental membrane and oxygen passing down it. Indeed, in some animals the conditions are particularly favourable, since the capillaries are arranged on the familiar counter-current principle, the streams of foetal and maternal blood running in parallel vessels but in opposite directions.

THE OXYGEN DISSOCIATION CURVE OF FOETAL HAEMOGLOBIN

Something better than this is evidently needed, however, for it is found that in both the maternal and the foetal blood adaptations occur to ensure a more efficient oxygen exchange. These adaptations result in an actual difference between the oxygen dissociation curves of maternal and foetal blood [1]. Typical curves are shown in figure 9 (for the goat) as well as the normal curve of the non-pregnant adult; it will be seen that, relative to this last, the foetal curve is moved to the left and the maternal to the right. This means that at any given oxygen pressure foetal blood becomes more highly oxygenated than maternal; in consequence, transfer of oxygen in the desired direction across the placental membrane is greatly speeded up.

The shift of the maternal curve is easily explained: it is due to an increasing acidity of the maternal blood as pregnancy proceeds. Experiments with normal adult blood have shown that an exactly similar rightward shift of the curve can be produced artificially by lowering the *pH* (figure 10); this is known as the Bohr effect and takes place without significant change in the shape of the curve. Furthermore, haemoglobin extracted as a pure protein from maternal (pregnant) blood has the same oxygen dissociation curve as that of normal adult haemoglobin; there is no evidence that there is any change in the adult haemoglobin itself during pregnancy.

The alteration in the foetal curve is a different matter. First of all, there is no evidence of an increase in the alkaline reserve of foetal blood

relative to adult blood, so we cannot invoke the Bohr effect in reverse; and, second, the foetal curve is obviously different in shape from the adult one, being more hyperbolic and less S-shaped (see figure 8 (F)). The change in shape of the curve is found in pure foetal haemoglobin solutions as well as in whole foetal blood, so it cannot be due to the nature of the foetal corpuscle or to any other environmental factor—it must be an intrinsic property of the haemoglobin itself.

This account of foetal and maternal dissociation curves has been somewhat oversimplified for the sake of brevity. The situation described is true of the goat and, in general outline, of most other species which have been investigated. Many readers would perhaps have been more interested in the state of affairs in man; this has not been described because surprisingly it is quite different from all other known cases. For while human adult and foetal haemoglobins possess different dissociation curves like the rest, the difference is in the reverse sense; that is to say, the foetal curve is the more S-shaped, and it is to the right of the adult. In whole human bloods, on the other hand, the foetal curve is to the left of the maternal as usual. So we must confine ourselves to the generalization that in all the cases so far examined the foetal and adult haemoglobin curves are different, but that the nature of the differences depends on the species.

FIGURE 1 – *The late Sir Joseph Barcroft, F.R.S., who carried out fundamental research on haemoglobin and foetal physiology for many years. He published a classical work entitled* Researches on Pre-natal Life *shortly before his death in* 1947.

These results have made physiologists interested in discovering whether there are any other observable differences between the foetal and adult haemoglobins derived from the same species, just as there are known to be differences between the adult haemoglobins of different species.

THE DENATURATION OF HAEMOGLOBIN

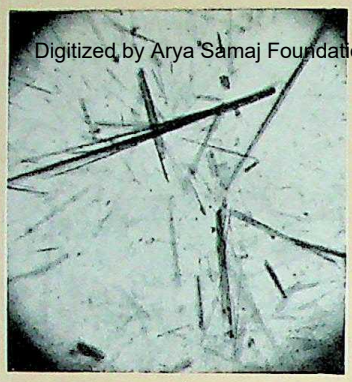
Strangely enough, some evidence of a difference between adult and foetal blood had been obtained over half a century before the earliest experiments on the oxygen dissociation curves of foetal blood, which were performed in the middle 1920's. The first record of a difference between adult and foetal bloods known to the present author is contained in an inaugural dissertation written for the University of Dorpat (Tartu) in 1866 by E. Körber [2]. He was examining the rate at which various haemoglobins were denatured in strongly alkaline solutions—a process which he was easily able to follow by watching the change in colour from the bright red of oxyhaemoglobin to the brown of alkaline haematin—and he found that foetal human haemoglobin, extracted from placental blood at birth, was denatured considerably more rapidly than adult.

Körber's work was not followed up until many years later. The idea that differences in properties between two proteins were reflections of a true structural difference developed slowly; only during the last half-century or so have proteins been credited with a definite molecular structure in the ordinary chemical sense of the term. The instability of proteins, their colloidal properties, and the difficulty of preparing them in a pure state, all militated against the acceptance of this idea; the conception of the individual protein as a molecule of specific and characteristic structure could become accepted only when techniques were perfected for handling proteins and for applying to them precise physical and chemical methods. So although Körber's observations of 1866, if made under suitably controlled conditions, should have been enough to establish a true molecular difference between foetal and adult haemoglobins, the problem has remained so far unsettled that even up to the present day it has been thought worth while to continue studying it.

SIMILARITIES AND DIFFERENCES BETWEEN FOETAL AND ADULT HAEMOGLOBINS

To keep the subject in a proper perspective it is first necessary to point out that the resemblances between adult and foetal haemoglobins are much more striking than the differences. Both have the same molecular weight (about 67,000) in all species so far studied. In both, the prosthetic

a



b

GURE 2 – *Crystals of sheep haemoglobin:* (a) *adult,* (b) *foetal.*
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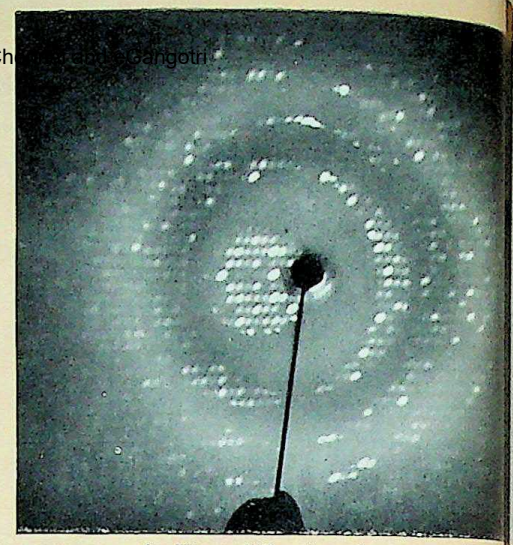
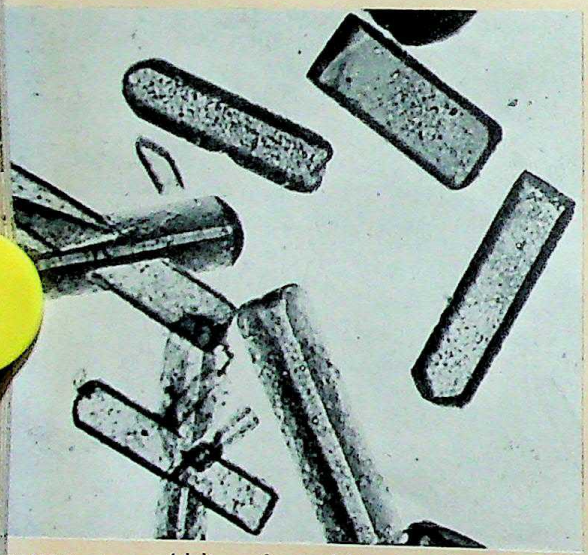


FIGURE 3 – *An X-ray diffraction photograph from a sheep haemoglobin crystal. Such photographs can be u discriminate between the structures of different protein cr*



IGURE 4 – *Adult methaemoglobin, crystallized from otassium phosphate.* (× 130)

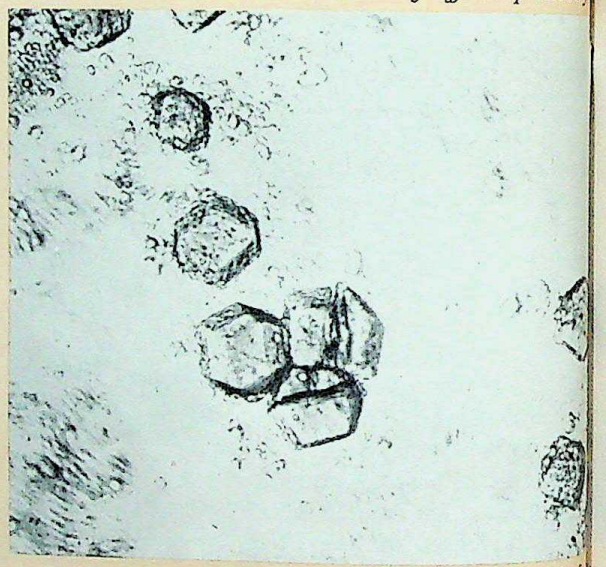


FIGURE 5 – *Foetal methaemoglobin, crystallized f potassium phosphate.* (× 110)

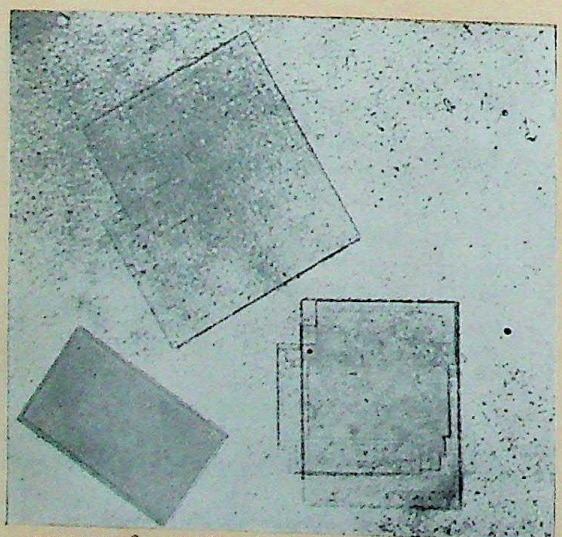


FIGURE 6 – *Adult reduced haemoglobin, crystallized from ammonium sulphate.* (× 110)

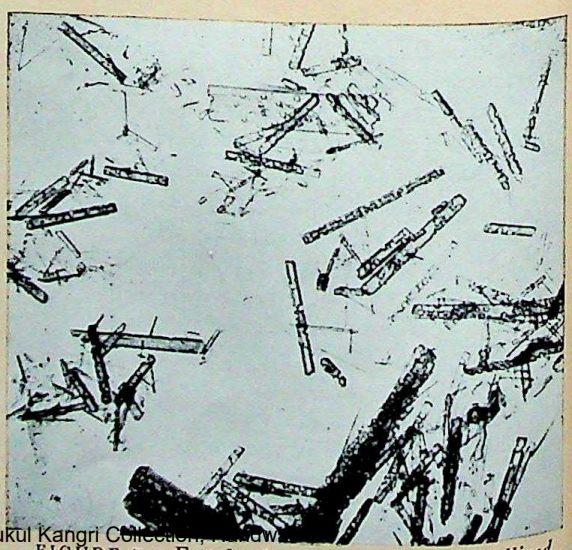


FIGURE 7 – *Foetal reduced haemoglobin, crystallized from ammonium sulphate.* (× 110)

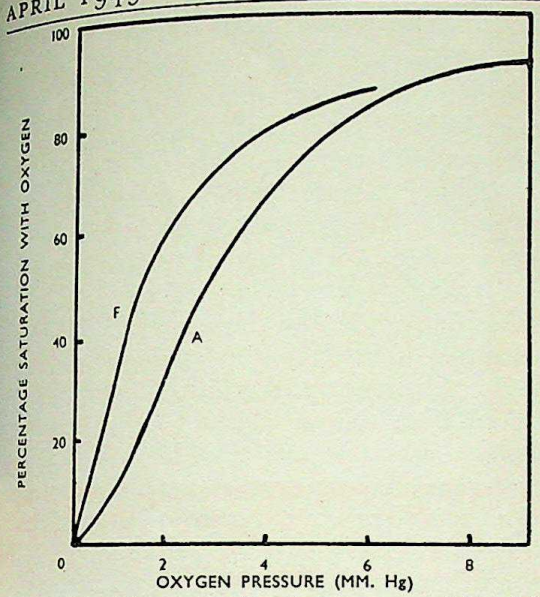


FIGURE 8 – *The oxygen dissociation curves of foetal (F) and adult (A) sheep haemoglobins;* p*H* 9·3, 19° *C.* (*After R. Hill,* 1935.)

group (to which the oxygen becomes attached) is the same iron porphyrin compound (ferroprotohaem, figure 11), and in both of them four of these haem groups are contained in each protein molecule. Any differences between the two must therefore be due to differences in the protein moiety, which is called globin; but in many of their properties the differences between the two proteins are very slight and hard to detect. Nevertheless they are real, as is shown below.

CHEMICAL DIFFERENCES

Let us begin by considering chemical properties, and first of all amino-acid composition. No complete analysis is available, but there is definite evidence of a difference between adult and foetal cow haemoglobins in methionine, *iso*leucine, and histidine content [3]. Again, the adult human haemoglobin molecule consists of five separate polypeptide chains, and the foetal of only two or three.

Körber's original experiments have been followed by other more thoroughgoing investigations of the alkaline denaturation of haemoglobin. For example, it was shown by Brinkman and Jonxis [4] that this reaction follows the unimolecular law, that is to say the logarithm of the amount of unchanged haemoglobin in the solution, plotted against the time, gives a straight line. Gently sloping lines (indicating high resistance to denaturation) were obtained for foetal bloods, and steep ones for infants'; while just after birth the line was kinked, indicating a mixture of about 80 per cent. foetal and 20 per cent. normal haemoglobin (see figure 12). These results were obtained with human haemoglobin, and the rabbit was found to behave similarly; in the goat and cow the situation is reversed, the foetal blood being less resistant than the adult.

PHYSICAL DIFFERENCES

We now turn to physical measurements. One of the simplest properties of a protein is its solubility, and the two types of haemoglobin have been

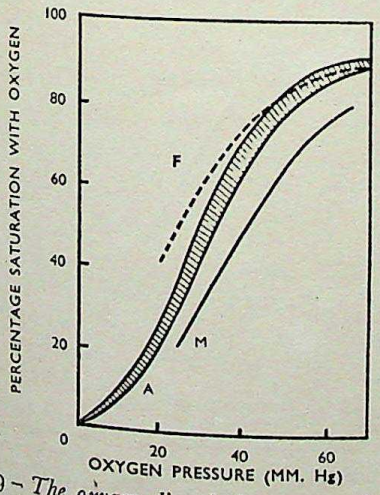


FIGURE 9 – *The oxygen dissociation curves of foetal (F) and maternal (M) goat's blood in the eighteenth week of foetal life (CO_2 pressure 50 mm). The limits of normality for adult (non-pregnant) blood are shown for comparison (A).* (*After J. Barcroft.*)

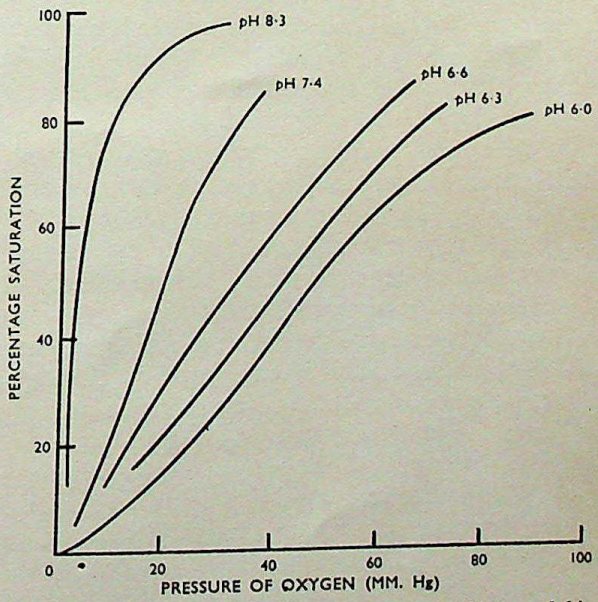


FIGURE 10 – *The oxygen dissociation curve of haemoglobin at various* p*H's, illustrating the rightward shift as the solution becomes more acid. It can be shown by replotting the curves, each on a suitable horizontal scale, that they are all S-shaped to about the same extent.* (*After Adair.*)

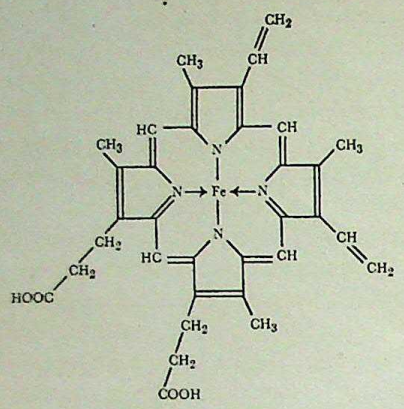


FIGURE 11 – *Ferroprotohaem—the prosthetic group of haemoglobin. In oxyhaemoglobin an oxygen molecule is attached to the central iron atom.*

found to differ most strikingly in this respect. For example, foetal cow haemoglobin is over six times more soluble in concentrated phosphate buffers than is adult [5]. Similar differences have been reported for sheep and human haemoglobin. The two kinds of haemoglobin also differ in electric charge; their isoelectric points are not the same, and so it is possible to separate them by electrophoresis.

Foetal and adult haemoglobins have been characterized by the rate of spreading of their monolayers on a water surface in the Langmuir trough. The quantity measured is the surface area occupied by a definite weight of protein under a certain pressure, and at a certain time after the moment at which the protein is placed on the surface. This area is a function of *p*H; it is a maximum at the isoelectric point. But at all values of *p*H the rate of spreading of adult human haemoglobin is much greater (nearly ten times) than that of foetal [4]. Furthermore the *p*H at which the spreading rate is maximal is different in the two cases—a consequence of the difference in isoelectric point already mentioned.

It was stated above that the molecular weight of foetal haemoglobin is the same as that of adult, viz. about 67,000. This statement is correct as far as it goes, but accurate determinations of osmotic pressure and of sedimentation-constant have shown that in very dilute solutions (below about 0·5 per cent.) some haemoglobins split reversibly into submolecules. In at least one species (the sheep) it has been found that adult and foetal haemoglobins behave differently in this respect; adult sheep haemoglobin remains unsplit even at high dilutions, while the foetal divides into two or even four submolecules.

BIOLOGICAL DIFFERENCES

One of the most delicate methods for differentiating between two proteins is to investigate their immunological specificities. The protein under test is injected into the bloodstream of an animal, which is thereby stimulated to produce an antibody protein; this antibody circulates in the serum and is capable of reacting with subsequent doses of the same foreign protein (or antigen) in a way calculated to protect the animal from the ill-effects of the latter—for example by forming a precipitate with it. Serum containing the antibody may be removed from the animal and caused to react with the antigen *in vitro*. As a method of identifying proteins this property of the living organism is of great value owing to its specificity; a foreign protein stimulates the formation of an antibody which will react with that same protein only, and with no other. As a matter of fact this specificity is not absolute; but it was quite sufficient in the present case to prove that adult and foetal human haemoglobins are different, for it was found [6] that an antibody produced in an experimental animal by the one failed to react with the other, and *vice versa*, though each antibody gave a precipitate with its own parent haemoglobin.

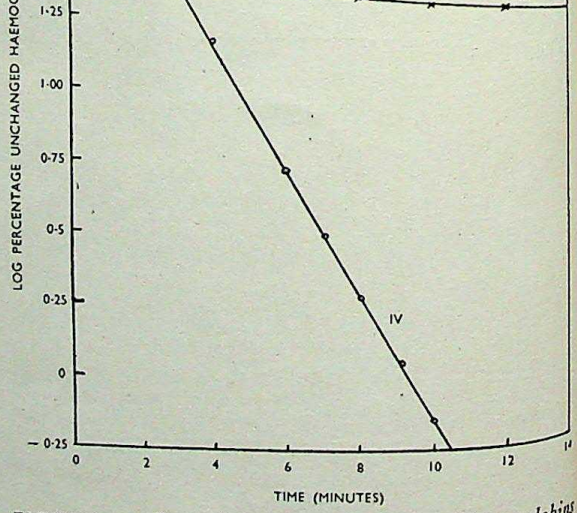


FIGURE 12 – *Rate of alkaline denaturation of haemoglobins from children of various ages, all measured at pH 12·20 and 25° C. I, from umbilical vein; II, 7-day child; III, 3-month child; IV, 7-month child. (After Brinkman and Jonxis.)*

SOME RECENT RESEARCH

A few years ago it was suggested to the present author by the late Sir Joseph Barcroft that the methods of X-ray crystallography might be used to study the foetal haemoglobin problem. Indeed, a number of earlier investigators had reported that the external crystalline forms of adult and of foetal haemoglobins of the same animal species were different, just as the crystals of adult haemoglobins of different species were known to be. In the present research the haemoglobins of adult and of foetal sheep were used, and it was clear from the start that, at any rate externally, the two crystal forms were quite dissimilar, adult haemoglobin forming triangular plates and foetal haemoglobin long, thin needles (see figure 2). It was later shown by X-ray methods [7] that the two types of crystal differed in symmetry and in space group, the adult ones being monoclinic and the foetal ones orthorhombic; furthermore the dimensions of the unit cells and the X-ray diffraction patterns were entirely dissimilar (figure 3). The results made it quite clear that the two sheep haemoglobins must possess different molecular structures. Since then it has been found [8] that human adult and foetal haemoglobins also differ in crystal form and symmetry.

Very recently a new controversy has sprung up. Jonxis [9] has been studying the disease *Erythroblastosis foetalis*, produced by Rhesus factor incompatibility in new-born babies; its principal effect is the destruction of a large proportion of the red blood corpuscles, often with fatal results. Jonxis believes that the foetal and adult haemoglobins do not occur together in the same corpuscle but that some corpuscles contain only foetal haemoglobin and others only adult; and he claims that in this disease the corpuscles containing foetal haemoglobin are broken down preferentially, the adult ones being more or less unaffected. The technique he used to demonstrate this is the rate of alkaline denaturation. His findings have now been criticized by Baar [10], who claims that the selective breakdown of certain corpuscles is due to a specific sensitization of those corpuscles by the Rhesus factor.

CONCLUSION

All these results, obtained by the use of many different techniques and with the haemoglobins of many different species, leave no room for doubt that foetal haemoglobin differs from adult haemoglobin of the same species. However, we still have no answer to a second and more important problem, namely the structural significance of the differences; for that matter we still know next to nothing about the significance of the differences between adult haemoglobins of different species. We do not even know of any differences which are entirely characteristic of the foetal forms. Foetal haemoglobin generally has a more hyperbolic oxygen dissociation curve than adult, but not always (e.g. in man); the rate of alkaline denaturation in foetal haemoglobin is in some species greater than in adult, in others less. At present it seems to be impossible to reduce the chaos to order, and we must suppose that most of the differences which have been observed are, so to say, accidental and irrelevant to the 'adult' and 'foetal' function of the haemoglobin. Meanwhile there are only a few isolated correlations; for example, it has been noted that in species where the foetal haemoglobin is less resistant to denaturation its rate of spreading in monolayers is greater than that of the adult form. We have no idea why this should be so, and it looks as if we are unlikely to get very much farther with such problems until a solution has been found to a much wider and more complicated one—in other words, until the general principles of protein structure become more clear.

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(No attempt has been made to provide a complete bibliography of the subject; comprehensive lists of references will be found in [1], [3], [5], and [7]. Figures 4–7 are reproduced by courtesy of Mrs. H. M. Jope.)

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Fungus diseases of fruit

R. W. MARSH

Although insects are as a rule the most destructive pests to which fruit trees are exposed, fungus diseases also are important. This is particularly so in Britain, where the growth of fungi is favoured by a humid summer climate. Roots, branches, leaves, and fruit are all liable to fungal attack. Study of the life-cycles and structures of the various parasites involved is leading to a clear idea of how and when fungicides can most effectively be used.

The attention paid to a parasite reflects the economic standing of its host. When insects and fungi attack the sloe and the crab-apple it is a visitation that we bear with equanimity, but the losses occasioned by parasites affecting our cultivated fruits are disheartening to the amateur grower and may be disabling to the professional. These attacks are often extremely destructive, because the fruit plantation provides an environment peculiarly favourable for the spreading of epidemics.

The natural defence mechanisms of plants are much less highly organized than those of animals. The non-woody organs (leaves, fruits, young shoots) are enveloped by a simple cutinized pellicle covering the outer walls of the epidermal cells. On the older woody structures this cuticularized epidermis is replaced by a periderm composed of layers of cork cells regenerated from within by a meristematic tissue, the phellogen. If the periderm becomes disrupted, exposing the thin-walled cortical cells under the phellogen, these cells frequently form a secondary phellogen, giving rise to a cork tissue, which may close the gap in the protective integument. The woody cylinder forming the axis of the branch or root is composed of specially modified cells unable to regenerate wound-cork but sometimes capable of forming a barrier by the secretion of gum.

These mechanical defences of the plant account only in part for any resistance it may show to parasitic attack. A fungus may gain a lodgment beneath the tegumentary layers but fail to make progress in parasitizing the plant cells, purely because their protoplasmic contents do not support the growth of that particular micro-organism. The nature of such innate resistance, which exercises an over-riding effect on the range of pathogenicity of the fungus, has not been elucidated. The degree of resistance often shows wide differences within the varieties of a single species of plant.

In the breeding and selection of cultivated fruits the aim has naturally been the increase and improvement of the edible product. Natural resistance to parasitism has been little prized in comparison with yield. Consequently there is a tendency for cultivated varieties to be more susceptible to diseases than their wild congeners. The effects of this susceptibility are magnified by the method of planting. The massing of like trees into large blocks is an essential requirement in commercial fruit production. In such a system of monoculture a specialized parasite finds an almost unlimited supply of food, permitting its multiplication at a rate far outstripping the capacity of natural enemies to hold it in check. In annual crops, infestations are commonly arrested by rotations, but interruptions of this kind will obviously occur very rarely in the culture of long-lived perennials such as tree fruits.

In most of the fruit-growing areas of the world the major parasites are insect. Fungus diseases of fruit are, however, widespread and numerous: they attain special importance in the United Kingdom, where the growth of fungi is favoured by the humid summer climate.

ROOT DISEASES

The duration of life of the British tree fruits—apple, pear, plum, and cherry—may be little less than that of soft-wooded forest trees: in consequence any root infection in an orchard has opportunities of wide extension in both space and time. The suberized layers of the bark normally safeguard tree roots against soil fungi, but one exception to this rule will be cited. The fungus *Armillaria mellea* is able to penetrate undamaged roots by driving a papilliform process, sometimes a quarter of a millimetre in diameter, directly through the bark. The penetration appears to be effected as a result of combined mechanical and chemical action. This mass invasion overwhelms the ability of the cortical cells to seal off the

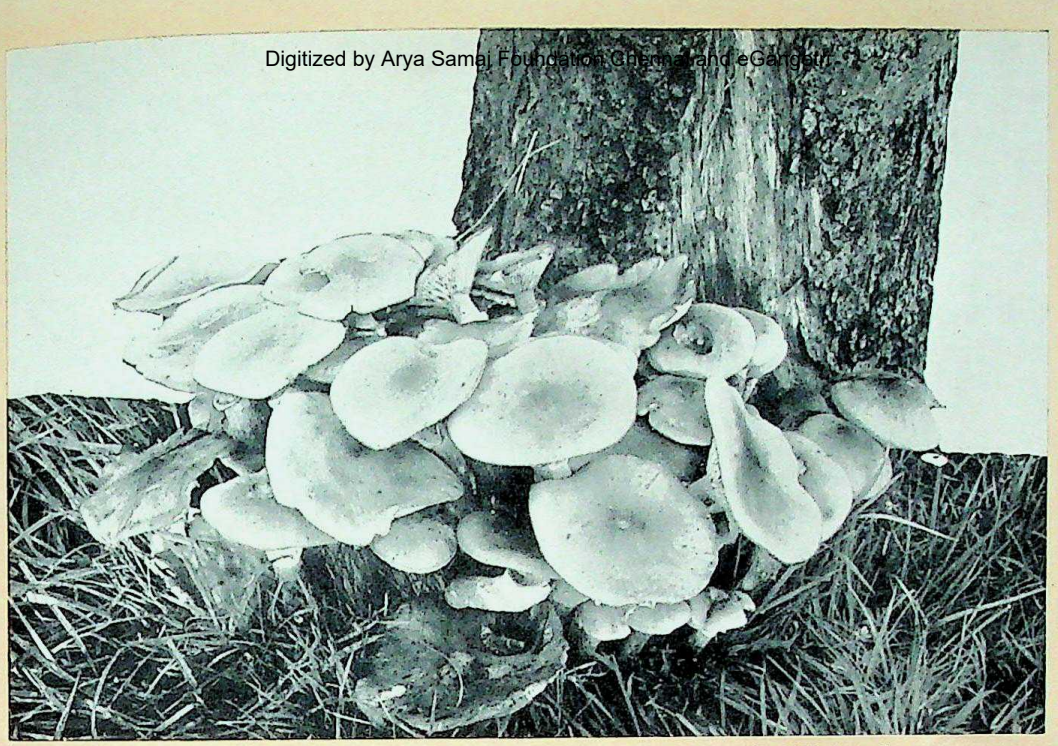


FIGURE 1 – *Fructifications of* Armillaria mellea *at the butt of a killed apple tree.*

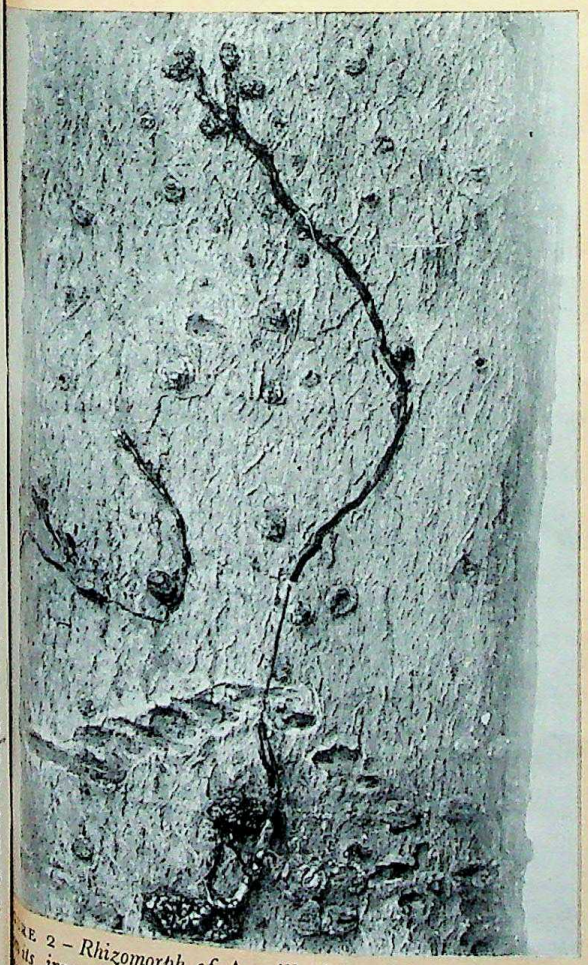


FIGURE 2 – *Rhizomorph of* Armillaria mellea *on a tree root. On its inner side the rhizomorph gives off branches that penetrate the bark.*

FIGURE 3 – *Cankers on apple shoots resulting from infection with* Nectria galligena.

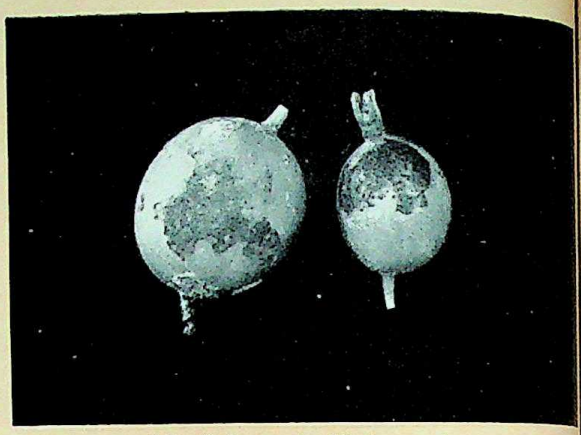


FIGURE 4 – *Mycelial growth of* Sphaerotheca mors-uvae *on fruits of gooseberry.*

FIGURE 5 – Venturia inaequalis *lesion causing scab spots on apple fruits.*

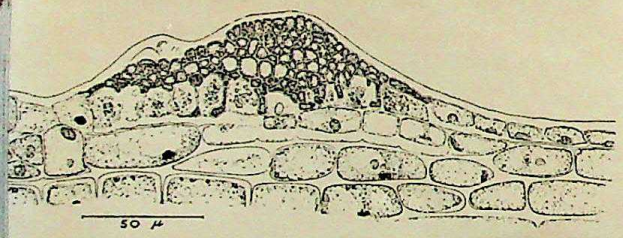


FIGURE 6 – *Lesion on a green shoot after six days' growth of* Venturia inaequalis. *The mycelium is passing from the subcuticular phase to the invasion of the epidermal cells.*

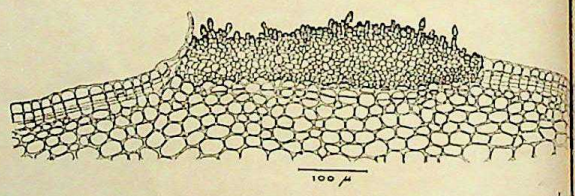


FIGURE 7 – *An infection approximately three weeks. The fungus stroma is circumscribed by the normal peri formed from the uninfected cells of the epidermis.*

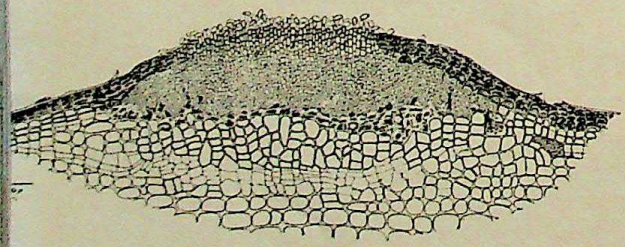


FIGURE 8 – *An infection in late October. The fungus has spread beneath the bark at the periphery of the lesion. A suberized layer is forming in the cortex below the stroma, but at the right of the section the fungus is spreading beyond this barrier.*

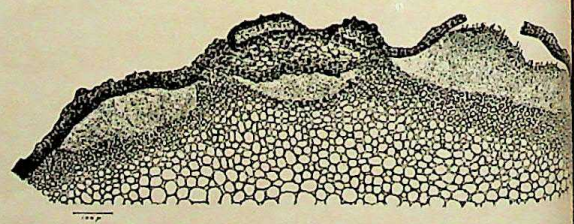


FIGURE 9 – *An infection in the following March. D the winter, subsidiary pustules have formed around and the original stroma (now shrivelled). Spores are formed the right-hand pustule, which has disrupted the bark.*

(*Figures 6–9 are reproduced by permission of the* Journal of Pomology and Horticultural Science.)

affected tissue, and the fungus continues its progress, destroying the interior of the root. When the growth of *Armillaria* has so far extended as to encircle the base of the trunk, the tree dies. The parasite then produces its fructifications at ground level—clumps of tawny-coloured toadstools, from which it derives its name of Honey Fungus (figures 1 and 2).

With the possible exception of the pear, all the fruit trees or bushes grown in the United Kingdom are susceptible to attack by *Armillaria mellea*. The cider orchards in the west of England show frequent examples of its ravages, particularly where tenancy agreements compel the farmer to plant a tree in a spot where wreaths of toadstools mark the grave of its predecessor. In commercial plantations the likelihood of introducing the fungus is small. There are instances where planting on cleared woodland or on the site of a hedge leads to outbreaks of root rot. Fortunately the fungus grows slowly, and prompt eradication of infected trees is normally an adequate safeguard against further spread. One problem still awaiting solution is the provision of a practicable method of freeing the soil from infestation.

DISEASES OF THE TRUNK AND BRANCHES

In the fungus diseases affecting the above-ground portions of the tree, the inoculum must necessarily be airborne. Commonly it takes the form of minute spores liberated in vast numbers from the fungus fructifications. As these spores fall in still air at a rate of approximately 1 cm per second they are widely disseminated by air currents, with the result that the trees in a fruit plantation frequently exist in an atmosphere charged with potential infection. The ability of the spores to initiate infection depends on the simultaneous occurrence of a number of circumstances favouring the parasite. For example, *Stereum purpureum*, the fungus causing silver leaf of plums and other members of the *Rosaceae*, can grow only in the older woody tissues of the tree. The spore cannot infect leaves or young shoots and is unable to bring about penetration of undamaged bark. It can initiate infection only when a broken branch or a pruning cut exposes an unprotected wood surface. A spore of *Stereum purpureum* reaching such a freshly made wound is sucked back into the exposed wood vessels, where it germinates, giving rise to a mycelium which spreads in the wood. A toxin produced by the infected tissues is carried to the leaves, where it causes the epidermal cells to split away from the tissues below. The air space thus formed imparts to the leaves the silvery sheen from which the disease is named. The fungus may continue its spread in the wood and eventually kill all or part of the tree, producing on the dead limbs the purple bracket-like fructifications which give rise to the next spore generation.

This progress of infection in silver leaf disease may be altered by the reaction of the host. Professor F. T. Brooks and his co-workers found that the growth of the parasite was sometimes arrested by a 'gum barrier' produced in the wood. Further, during the months of June, July, and August this gum barrier forms with sufficient rapidity below an exposed surface to bar the entrance of the fungus. In addition to this seasonal effect there are also wide varietal differences. Many plum varieties show the power of natural recovery from silver leaf attack, and the disease, although still dangerous on certain varieties, is now much less feared than in the inter-war years.

A further stage in the augmenting of paths of infection is shown by the life-cycle of *Nectria galligena*, the fungus causing canker of apple and pear. *N. galligena* mainly parasitizes the woody tissues, but it also invades the cortex and can develop to a limited extent on the fruit. Like *Stereum purpureum* it is a wound parasite, but the *Nectria* spores can infect not only gross wounds, such as broken branches and pruning cuts, but the minute crevices occurring in the leaf scars on the shoots. When the leaf is shed, the exposed tissue of the scar dries and cracks. *Nectria* spores lodging in the cavities readily germinate, to form hyphae penetrating the cortical cells of the shoot. In the autumn months these cells are relatively inactive and often fail to form a phellogen in time to limit the growth of the fungus. A second phase of infection occurs in the spring, when the paths of entry are the bark-cracks that accompany the swelling of the buds.

The growth of the canker fungus may girdle a young shoot within a few weeks and bring about the death of the distal portion. On older branches the canker forms a lenticular lesion, on the margin of which cork barriers are laid down in the cortex. The ability of the fungus to invade the cells of the wood enables it to outflank these barriers, and repetition of this sequence gives the canker its corrugated surface (figure 3). Between the successive ridges the fructifications of the fungus appear, first as naked masses of summer spores (conidia), then as red thick-walled perithecia enclosing the winter spores (ascospores). The conidia are

dispersed by spattering in wind-blown rain: the ascospores are shot out to a distance of 3 cm and disseminated by air currents. The overlapping of production of the two forms of spores maintains a supply of inoculum throughout the year.

While in combating the silver leaf disease it is practicable to treat wounds and pruning cuts individually with a protective paint, such treatment is not applicable to the innumerable microscopic ports of entry of the canker fungus. A limited degree of protection has been conferred on leaf scars in young trees by autumn and spring spraying with copper-containing fungicide, but the more hopeful methods of checking canker appear to lie in the buttressing of the natural defence mechanisms of the tree. The varietal range of susceptibility to canker is a wide one. Apple trees of the variety Bramley's Seedling, for example, will remain almost free from infection on a site where trees of James Grieve are rapidly killed. This inherent varietal resistance may be modified by habitat: trees on heavy clay soils or those receiving a high level of nitrogenous manuring are specially prone to canker. The nitrogen uptake of a tree is amenable to control, and a frequently successful practical device for reducing canker attack is the grassing-down of the apple plantation.

DISEASES AFFECTING LEAVES AND FRUIT

The appearance of the reproductive stage in fungi often marks the end of a phase of vegetative growth. In the wood-infecting species vegetative growth may be prolonged, with the consequence that the parasite spreads relatively slowly from tree to tree. By contrast, a foliage-infecting fungus, rapidly exhausting the limited resources of an individual leaf, starts spore production after a very brief vegetative phase. These spores spread infection to other leaves of the same host, providing the means for extensive multiplication and spread within a single summer.

The parasitism of the leaf fungi is much less sporadic than that of the wood pathogens. Commonly it is an annual recurrence which, in commercial fruit-growing, must be combated by routine protective treatments. In the absence of these measures epidemic outbreaks of disease are inevitable.

An example of such epidemic spread is afforded by the American mildew of the gooseberry, caused by *Sphaerotheca mors-uvae*. This imported parasite reached Ireland in 1900 and England about 1906. On the leaves it forms a felt of mycelium, with haustoria below penetrating the epidermal cells, and chains of spores above. Later the fruits and shoot tips are similarly disfigured, the fungal coating becoming darker with age (figure 4). In this mycelial layer on the shoot-tips are produced the perithecia, which endure throughout the winter and give rise to the ascospores responsible for renewing the infection in spring.

As soon as the American mildew reached the British Isles its importance was realized by Professor E. S. Salmon, who pressed for legislative measures to safeguard the gooseberry crop. In 1907 the Destructive Insects and Pests Act, the first English statute aimed against a fungus disease, became law. Under this act orders were made for the compulsory destruction of diseased bushes, but as no provision was made for State compensation the orders proved unworkable. The 1907 Act did, however, provide the basis for many subsequent orders, which now form an essential element in the resources available for plant disease control.

American mildew was eventually curbed by the use of chemical therapeutics. The basic difficulty in the use on higher plants of materials toxic to fungi is that the fungus itself is a plant and consequently the difference in levels of toxicity to host and to parasite is often small. It is not generally practicable to kill a fungus once it is within the plant tissue, but by applying a fungicide to the exterior of the plant the entry of the parasite may be prevented. Protectant fungicides for outdoor use in a wet climate must necessarily be highly insoluble, but the germination of the spore lodging on the treated surface is inhibited by the soluble products arising from the reaction between the prophylactic and the spore excretions.

The fungicides used on the gooseberry plant are commonly sulphur and polysulphides. A complicating factor is that reactions between the gooseberry foliage and the sulphur may occur, sometimes with phytocidal effect. Certain of the choicer dessert varieties are readily defoliated by contact with any form of sulphur, but the mechanism of this effect remains obscure.

The fungus disease of greatest economic importance in British fruit-growing is that caused by the apple scab fungus *Venturia inaequalis*. This manifests itself in summer by dark powdery spots on leaves and fruits (figure 5). These blemishes are not more than skin deep: the fungus spreads beneath the cuticle but does not penetrate the epidermal cells. When, however, in late summer infections reach the young green shoots, the morphological structure of the lesion is profoundly

affected by the development of the periderm. As the normal formation of the phellogen starts, *Venturia inaequalis* becomes more actively parasitic and invades the meristematic epidermal cells (figure 6). Meanwhile the surrounding healthy epidermis is being replaced by the periderm, and a stage is soon reached at which the growth of the parasite is circumscribed by the newly formed external cork (figure 7). Beneath these cork cells the thin-walled phellogen remains active, and by invading this tissue the fungus extends its growth. Thus the infection becomes established under the protection of the bark (figure 8).

Venturia inaequalis grows even at 5° C, and is able to build up during the winter an annular stroma under the bark surrounding the original lesion. Increase in thickness of this stroma ruptures the bark in spring, disclosing a spore-bearing layer immediately beneath (figure 9).

The spores of the apple scab fungus are not dispersed by dry wind, but rain loosens their attachment to the stroma and they are disseminated in the wind-blown drops. If a spore lodges on an unsprayed apple leaf and remains wet for approximately six hours, it germinates and sends an infection thread directly into the cuticle. Within three weeks the lesion on the leaf may produce spores which infect more leaves, then fruit, and eventually the current year's shoots. This cycle is not the only means of perpetuation of the fungus: it persists during the winter in the fallen leaves, where it produces ascospores, which are shot into the air during wet periods in the spring.

Rain is indispensable to the establishment and dissemination of the scab fungus: in the high-rainfall areas of this country the disease is so favoured that commercial apple production becomes impossible. Elsewhere scab is fought by spray treatments employing the same principles of leaf and fruit protection as those described for American gooseberry mildew. In the apple, the period between bud-burst and fruit-maturity is much longer than in the gooseberry, and the spray programme is correspondingly more protracted. If all the susceptible organs of a tree are given a complete spray covering in early summer, the continued unfolding of new leaves will soon supply more unprotected surfaces liable to infection during wet periods. The ideal timing of spray applications to anticipate rainfall by approximately twenty-four hours would be feasible only if rainfall could be accurately forecast at least two days in advance. Under English conditions some other basis for the choice of dates of spray application must be found. The greatest danger of scab infection occurs, first, in the month before blossoming, when the flower trusses and adjacent leaves are expanding, and, second, at the petal-fall period, when the extension shoots and the young fruits are both developing rapidly. Three or four tenacious fungicidal spray deposits, spanning the interval between mid-April and late June, are the normal requirements for successful control.

The fungicide in general use is lime-sulphur (sulphur dissolved in a mixture of calcium polysulphides), applied by spraying in weak aqueous solution (1–3 per cent.). In general, the natural draining-off of surplus spray liquid from the leaves furnishes a safeguard against damage by excessive deposit. As this method involves the use of at least 1½ tons of water per acre for each spraying, attempts are being made to replace water-borne sprays by the use of concentrated fungicides dispersed as droplets in large volumes of air. Such an air-blast application would possess no inherent safeguard against overdeposition and is dependent on the adoption of fungicides less phytotoxic than lime-sulphur. A satisfactory material might be found among the numerous recently developed organic fungicides, which include derivatives of thiocarbamates, quinones, quinolines, and imidazolines.

The adoption of air-dispersed sprays would demand further modification of the spacing of plantation trees, already much changed in the past twenty-five years by the requirements of the conventional methods of spraying. Choice of varieties in large-scale fruit growing has long been limited to those on which the control of parasites is practicable. The necessity for checking the spread of fungus diseases, added to that of controlling insect pests, is the largest single factor in determining the annual maintenance cost of a commercial plantation, and now exerts a profound influence on the whole pattern of fruit production.

Recent developments in the chemistry of perfumes

R. W. MONCRIEFF

With the advance of exact knowledge, many an empirical art has become a branch of applied science. This metamorphosis is now occurring in perfumery. Until comparatively recently all perfumes were obtained from natural sources, and their successful extraction and blending were the closely guarded secrets of a few families. Nowadays chemistry is probing the secrets of smell, analysing and synthesizing Nature's perfumes, and evolving new products for the use of the perfumer's skill. Some of the most important developments are here described.

Much the greatest part of any perfume as purchased ready for use is a diluent. Substances which are powerfully odorous are generally only slightly soluble in water, but are readily soluble in fatty liquids and in some other organic solvents. This is understandable, because in order to stimulate the olfactory sense the odorous substance must be able to dissolve in the lipoid or fatty tissues in the olfactory cleft high up in the nose. It is true, of course, that the powerful odorants used in making perfumes are not applied in the liquid form to the interior of the nose; they are, however, invariably volatile, and particles or droplets of them find their way into the nasal orifices of anyone near, who consequently experiences the sense of smell. The substances used in perfumery have such very powerful odours that they have to be diluted very considerably when compounded in perfumes, and the substance used as a diluent in the old days was olive oil. Perfumes made with an olive oil base are known as *huiles antiques*. Olive oil is suitable for this purpose in so far as it is a good solvent for many powerful odorants, particularly for the natural essential oils of flowers, and itself has only a bland odour. It has, however, been superseded as a perfume diluent by ethyl alcohol, which possesses the following advantages over olive oil:

1. It is colourless, and the perfumer may thus give any desired colour to his product.
2. It is completely volatile and leaves no residue, so is very suitable for application to clothing.
3. Its odour is pleasant and stimulating but not sufficiently strong to interfere with that of the perfume.
4. It is a better solvent for some perfume materials than olive oil.
5. It is not subject to cloudiness on cooling as is olive oil.

One might add that the use of olive oil in the manufacture of perfumes would almost certainly not be permitted at the present day, in view of the world shortage of edible fats.

Of recent years considerable use has also been made of isopropyl alcohol since it became available in large quantities, its main advantage lying in its freedom from excise duty. Its odour is unfortunately much more obtrusive than that of ethyl alcohol and not nearly so pleasant, so that its use has been confined to the less expensive kinds of perfumes and in particular to cheap products of the eau-de-Cologne type.

ANIMAL PERFUME MATERIALS

As far back as the history of perfumery goes, extensive use has been made of certain animal products of sexual function, notably musk and civet. The male musk deer, *Moschus moschiferus*, a harmless night-wandering inhabitant of the rhododendron thickets of the Himalayas, carries a sac about the size of an orange in the front of the abdomen, and this sac fills with a substance rather like moist gingerbread in consistency. The deer is killed, the sac is removed and dried, perhaps in the sun, and the contents are sold as 'musk in the pod.' In nature the function of the powerfully odorous musk is to guide the female to the male. Musk has a soporific effect and also, as has been found recently, a hormone-like action in stimulating male sex-activity. It is also a powerful fixative for vegetable perfumes, i.e. it makes them more persistent. Women almost invariably prefer perfumes that contain musk.

Civet is obtained from the civet cat, *Viverra civetta*, both sexes having a glandular secretion near the genital organs. As the civet can be spooned out without hurt to the animal, the cats are kept in captivity, and it is said that they are

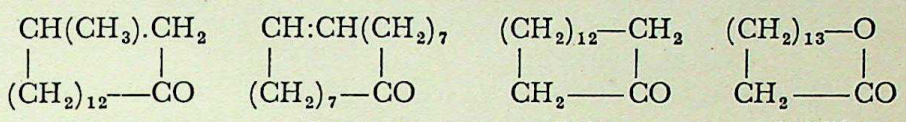
teased to stimulate the production of more civet. Civet has an odour that is partly musky but also disgustingly faecal; it is remarkable that in highly diluted alcoholic solutions it should have a sweet odour. Like musk, civet is a powerful fixative.

Either musk or civet has been a *sine qua non* of good perfumes until very recently, and it was during an investigation of these products that the most striking developments were made in the chemistry of perfume materials.

In 1926 Ruzicka succeeded in isolating the essential odoriferous constituent of natural musk; it proved to be a ketone, to which the name muscone was given. Ruzicka was able to determine the structure of this ketone as 3-methyl cyclopentadecanone. Here was an amazing discovery, for hitherto it had been believed that such large carbon atom rings were highly unstable. Benzene with its six-carbon atom ring is very stable, and cyclic compounds containing as many as eight ring-carbon atoms were well known, but it was believed that as the number of carbon atoms in the ring increased the stability rapidly decreased. Up to 1926 any organic chemist confronted with the task of preparing a compound containing a ring of fifteen carbon atoms would have unhesitatingly rejected it as impossible; yet Ruzicka found that muscone, the odoriferous essential of musk, which had been widely known and used for thousands of years, incorporated such a ring. More than that, he subsequently synthesized it. Turning his attention to civet, he isolated the essential odoriferous constituent—another ketone, which he termed civetone and which proved to be Δ^9-cycloheptadecenone, that is, it contained a seventeen-carbon atom ring. This most unusual macrocyclic carbon ring structure may perhaps have been reserved by Nature for the special function of sex attraction.

MACROCYCLIC SYNTHETICS

Once the door had been opened by the masterly researches of Ruzicka, and the two oldest and most valued perfume materials had been identified and synthesized, a large number of synthetic materials similar in general structure to muscone and civetone, but not found in nature, soon made their appearance. Two such substances, Exaltone and Exaltolide, have been marketed on account of their beautiful musk-like odours. Exaltone is cyclopentadecanone, a cyclic ketone with a fifteen-carbon ring, and Exaltolide is pentadecanolactone, the internal anhydride of ω-hydroxypentadecanoic acid. The structural formulae of these substances show the very striking resemblance between the natural muscone and civetone and the new synthetics:



Muscone *Civetone* *Exaltone* *Exaltolide*

In the years that followed Ruzicka's interesting discoveries many other macrocyclic compounds were synthesized, or were found in natural products such as angelica root oil, but the next major advance came from Hill and Carothers. They investigated the influence of ring size on the odour of macrocyclic ketones, lactones, anhydrides, and carbonates. Of these, the lactones and the ketones had the finest and most useful odours, and it is instructive to note how the odour changed with increasing ring size. This is shown in the following table.

Total Atoms in Ring (carbon and oxygen)	*Ketone* $(CH_2)_n$ CO	*Lactone* $(CH_2)_n$ O—CO
5 ..	Bitter almonds, menthol	Fruity
6 ..	Bitter almonds, menthol	Faint
7 ..	Transitional	Faint spicy, floral
8 ..	Transitional	—
9–12 ..	Camphoraceous	—
13 ..	Cedar wood, musky when dilute	—
14 ..	Musk	Musk
15 ..	Pine musk	Ambergris
16 ..	Transitional	Musk
17 ..	Civet	Civet
18 ..	Faint civet	Faint
19 ..	Faint	—

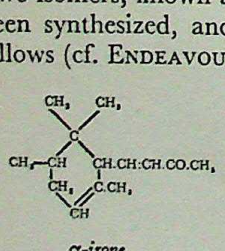
It seems clear that the musk odour reaches a maximum at 15–16 atoms in the ring. Many macrocyclic esters were prepared by Carothers, and, in their case too, members with fifteen-atom rings, such as undecamethylene oxalate and ethylene undecanedicarboxylate, had musk-like odours.

These researches have revealed the existence of natural products containing large rings of 15–17 carbon atoms, have made it possible for the perfumer to obtain in a pure state the active constituents of

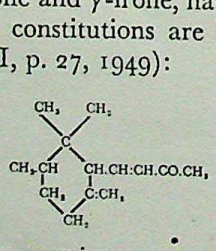
musk and civet which normally contain only 1–2 per cent. of active ketone, and should make unnecessary the destruction of the musk deer. At the same time they have enormously increased the range of sex-attractive materials at the disposal of the perfumer.

VIOLET PERFUMES

The smell of violets has always been esteemed, perhaps partly because of its elusive quality. We gently smell the flowers and are enchanted; but plunge our nose into a bunch, and the odour has gone. Rimmel, who classified the pleasant odours according to their empirical likenesses, grouped orris root, cassie, and mignonette with violets The violet odour is indeed found in orris root, and, owing to the extreme difficulty of obtaining any considerable quantity of oil from violet flowers, Tiemann and Krüger in 1893 isolated the active odoriferous principle from orris root, the dried rhizomes of *Iris florentina*. Irone, the active principle, proved to be a ketone, and although the generalities of its constitution have long been understood there have until very recently been uncertainties about its exact structure. The October 1947 issue of *Helvetica Chimica Acta* contained a paper by Ruzicka, written in collaboration with some of the chemists of Firmenich et Cie. (late Chuit Naef et Cie.), in which a synthesis of irone is described, and very curiously the same issue contains another paper by Naves and his collaborators, of L. Givaudan et Cie., describing the same synthesis by a very similar route. It is strange that a problem of perfume chemistry which engaged the active attention of perfumery chemists for fifty years should have been solved simultaneously and independently by two schools of workers. Irone, which had until quite recently been suspected of having a seven-carbon atom ring, proves to have the much more common six-carbon ring. Two isomers, known as α-irone and γ-irone, have been synthesized, and their constitutions are as follows (cf. ENDEAVOUR, VIII, p. 27, 1949):



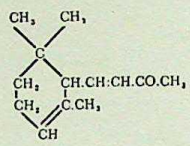
α-irone



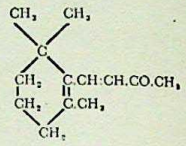
γ-irone

Now that irone has been synthesized it may be used to a much greater extent in compounding violet perfumes, but meanwhile many other interesting products with different nuances of the violet odour have been prepared and employed.

Tiemann and Krüger came very close to the synthesis of irone when they attempted to make it from citral and acetone. They actually obtained the ionones, the constitution of which, long known, is very similar to that of irone:



α-ionone



β-ionone

The ionones have violet odours, α-ionone a sweet odour similar to orris root and β-ionone one nearer to natural violet. Practically all violet perfumes, especially those of lower price, contain ionones. The better qualities also contain a trace of true violet-leaf oil, of which the active constituent is 2:6-nonadienal, an unsaturated straight-chain aldehyde.

A typical member of a most interesting series of acetylenic esters, discovered by Moureu and Delange, is methyl heptin-carboxylate,

$$C_5H_{11}.C : C.COOCH_3.$$

It possesses a fine and persistent fragrance of violets when suitably diluted, but when concentrated its odour is strong, sharp, penetrating, and disagreeable. It has been extensively used in perfumes of many kinds and is almost invariably used in all but the cheapest violet perfumes. A homologue, ethyl decin-carboxylate, which has recently appeared, has a mignonette and leafy odour and is less pungent than the heptin-carboxylates.

Another substance which unexpectedly has an odour of violets is γ-propyl-pyridine. When it is remembered that pyridine itself has a rank, unpleasant smell, this may be taken as an illustration of the difficulty that attends the correlation of odour with chemical constitution. A further example is α-propyl-pyridine, which has a general flowery odour with no particular resemblance to violets.

ACETALS AND KETALS

Aldehydes constitute one of the most important classes of perfumery compounds. One has only to think of α-amyl cinnamaldehyde, known as jasmin aldehyde; of piperonal with its cherry-pie odour; of anisic aldehyde or *aubépine* with its hawthorn odour; of vanillin; or of hydroxycitronellal, a valuable synthetic in which citronellal hydrate predominates and which has a fine lily-of-the-valley

odour. Lauric aldehyde, made from coconut oil, has such a powerful high note that it is used, in traces only, to supply the distinctive tone of almost every well-known perfume of the modern French type. The aldehyde group has such brilliant osmophoric qualities that one might inquire why in perfumery aldehydes are normally converted into acetals. The answer is that aldehydes are unstable, subject to atmospheric oxidation, and liable to polymerize. The acetals are generally of higher boiling-point than the corresponding aldehydes, and this makes them more persistent as perfume constituents; they are also very much more stable. Acetal formation consists of protecting the aldehyde group by reaction with an alcohol, e.g.:

$$\underset{\textit{aldehyde}}{RCHO} + \underset{\textit{alcohol}}{2EtOH} \rightarrow \underset{\textit{acetal}}{RCH(OEt)_2} + H_2O.$$

Semi-acetals may also be made according to the reaction:

$$\underset{\textit{aldehyde}}{RCHO} + \underset{\textit{alcohol}}{EtOH} \rightarrow \underset{\textit{semi-acetal}}{RCH\begin{matrix}\diagup OEt \\ \diagdown OH\end{matrix}}$$

As an example of their use we may consider *p*-isopropyl-α-methyl-hydrocinnamaldehyde, which has an intense blossomy cyclamen-like perfume, but which on exposure to the atmosphere for twelve days oxidizes to the extent of some two-thirds, the odour becoming weak and sour. When the aldehyde is converted into the semi-acetal the odour is retained and is not appreciably changed on similar exposure to air.

Aldehyde or Ketone	*Alcohol*	*Odour of Acetal or Ketal*
Phenyl acetaldehyde	Ethylene glycol	Rose
Phenyl acetaldehyde	1, 2-Dihydroxy butane	Hyacinth
Phenyl acetaldehyde	2, 4-Dihydroxy-4-methyl pentane	Mignonette
Heptaldehyde	Glycerol	Mushroom
Hydratropic aldehyde	Ethylene glycol	Fine odour of earth and mushroom
Hydratropic aldehyde	2, 4-Dihydroxy-4-methyl pentane	Herbaceous, mignonette
Cinnamaldehyde	Ethylene glycol	Agreeable, like oil of cinnamon
Di-isopropyl-ketone	Catechol	Rose-geranium
Di-isobutyl ketone	Catechol	Honey
Methyl amyl ketone	Catechol	Jasmin

In a similar way ketals may be prepared from ketones and an alcohol. Very interesting perfumery materials are to be found among these acetals and ketals, particularly when the alcohols used are dihydric (glycols). The above combinations well illustrate the variety of odours that may be obtained, and it should be remembered that the field is still largely unexplored and probably fertile.

Book reviews

CHEMISTRY DURING 1947

Annual Reports on the Progress of Chemistry for 1947. Vol. XLIV. *Pp.* 327. *The Chemical Society, London.* 1948. 20*s. net.*

Since 1904 The Chemical Society has rendered a valuable service to chemists by the publication of its Annual Reports. Some two years ago the Society began a new venture, Quarterly Reviews, in the hope that it would enable chemists to keep up to date. In some spheres there was a feeling that with Quarterly Reviews the need for Annual Reports had ceased. Actually there is a place for both publications, and a survey of the contents of the volume under review makes this quite clear.

In the section devoted to General and Physical Chemistry there are excellent articles on the kinetics of electrode processes and on far ultra-violet spectra and related topics. The topics dealt with in Inorganic Chemistry remind us that this subject is changing from a descriptive and preparative science to one concerned with valency, structure, and reaction mechanisms. Recent work on organic compounds containing fluorine, and recent advances in aromatic chemistry, are discussed in the section dealing with organic chemistry. Modern work on the terpenes is also reported, and further developments in the steroid field are described. Results of outstanding chemical and biological interest are summarized in an account of marrianolic and doisynolic acids.

In the thirty-eight pages devoted to biochemistry topics are selected which, notwithstanding their importance, have been inadequately reviewed elsewhere. This underlines one important function of the present volume. Finally a series of interesting articles under the general heading of Analytical Chemistry completes a publication which should be in the hands of every chemist.

W. WARDLAW

HISTORY OF ALCHEMY

Ambix: The Journal of the Society for the Study of Alchemy and Early Chemistry, *edited by F. Sherwood Taylor. Vol. III, Nos. 1 and 2. Pp.* 67. *Taylor and Francis Limited, London.* 1948. 48*s.* net.

The Society for the Study of Alchemy and Early Chemistry has as its object the scientific and historical study of the branches of learning named in its title. Meetings are held for the reading of papers or for discussions. The annual subscription is £2 2s. and should be sent to the Hon. Treasurer, Denis I. Duveen, F.R.I.C., c/o Ashe Laboratories Limited, 120 Victoria Street, London, S.W.1. Members of the Society receive the journal *Ambix* free of charge. The subscription to non-members, libraries, and institutions for one year (four issues) is 48s. post free; it should be sent to Messrs. Taylor and Francis Limited, Red Lion Court, Fleet Street, London, E.C.4. Applications for membership of the Society should be made to the Hon. Secretary, Dr S. F. Mason, Museum of the History of Science, Broad Street, Oxford. The present issue of *Ambix* contains articles on 'Chemical and Technological References in Plutarch' by E. O. von Lippmann, 'Rhetorical and Religious Aspects of Greek Alchemy' by C. A. Browne, *Le Livre de la Très Sainte Trinité* by D. I. Duveen, 'The Chemical Work of Paracelsus' by T. P. Sherlock, and a review of C. G. Jung's book *Psychologie und Alchemie* by G. Heym. The Plutarch article will bring to many readers of ENDEAVOUR warm recollections of Edmund von Lippmann, whose death in 1941 deprived the world of learning of a genial and accomplished scholar; von Lippmann was always ready to place his vast store of knowledge at the disposal of other students, and was charmingly modest about his own achievements. His book *Die Entstehung und Ausbreitung der Alchemie* must long remain invaluable to all serious historians of early chemistry. Sherlock's article, too, is unhappily posthumous; it supports Darmstädter's view that Paracelsus is not to be regarded as one who freed chemistry from the chains of alchemy or as a modern experimenter, but that his real contribution to the progress of chemistry is in the new direction that he gave to its activities in consequence of his whole philosophic outlook. Sherlock believed, however (and many will believe with him), that there remains a doubt as to whether Paracelsus really had quite as systematized a philosophy as Darmstädter attributes to him. Certainly Paracelsus performed a very great service in presenting the world, for the first time, with something like a system of chemistry, extending the scope of the science to the sum total of all operations by which man modifies the materials around him.

The Society for the Study of Alchemy and Early Chemistry is to be congratulated upon the very valuable work that it is doing, and deserves the active support of all those interested in the history of science.

X-RAY CRYSTALLOGRAPHY

Fourier Technique in X-ray Organic Structure Analysis, *by A. D. Booth. Pp.* 106, *with several half-tones and line drawings. Cambridge University Press.* 1948. 12*s.* 6*d. net.*

About twenty-five years ago the possibility was seen of reconstructing the atomic arrangement of solids by inserting the intensities of the diffracted X-ray beams into a Fourier summation. Since that time great progress has been made, both as regards the basic principles of the method and in the technique of calculation. This progress is described in numerous publications scattered among a diversity of journals, but the author of this book has compressed into a hundred pages a fairly complete literary survey, providing the first comprehensive account of the methods available. Also included are valuable contributions by the author himself, made during a prolonged study of this problem.

The description of how to obtain and measure the diffracted X-ray beams is left to the many existing accounts of this subject, and, after a brief description of the scattering of X-rays by crystalline matter, the present volume is devoted entirely to the handling of such values once they have been obtained and suitably corrected.

The essentials and limitations of all the possible Fourier representations are discussed, and simple numerical examples are given to facilitate the reader's progress. Nearly half the book is devoted to a description of methods and machines for carrying out the laborious computation involved, and it is felt that this section will do much to encourage those to whom the difficulties of such a procedure seem at first to be insurmountable. Throughout, the work stresses the importance of the accuracy with which atomic position can be 'fixed' within the structure, this knowledge being essential when information is sought regarding the chemical nature of the bonding.

The reader is assumed to have a basic knowledge of geometrical crystallography and the theory of space-groups, and this may present some difficulty to the student from other branches of science. The diagrams are well produced and the contents adequately indexed; it is certain that the book will be welcomed by all engaged in this specialized field.

H. F. KAY

THE CAUSES OF FLOWERING

Vernalization and Photoperiodism, a Symposium, *by A. E. Murneek and R. O. Whyte, assisted by thirteen others. Pp. viii* + 196, *with* 12 *plates and* 26 *figures. Chronica Botanica Co., Waltham, Mass.* 1948. 25*s. net.*

The phenomena of vernalization and photoperiodism were first precisely described, within a few months of each other, some thirty years ago. Since then a great deal of work has been done on both phenomena, yet neither of them is properly understood. During the war, in the United States, Britain, Germany, Belgium, and the Soviet Union experimental botanists were independently working on the causes of flowering. When the flow of scientific information between countries was resumed it was evident that great advances had been made, often converging toward the same conclusions, by men who had known nothing of each other's work.

This symposium, which is due to the energy and enterprise of Dr. Verdoon, of the Chronica Botanica Press, brings together the results of some recent work and puts them against the background of the last thirty years. There are chapters on the history of vernalization and photoperiodism, from which it appears that both were adumbrated nearly a century ago. K. C. Hamner writes on hormones in relation to flower production; H. A. Borthwick on the effects of radiation of different wavelengths; R. H. Roberts on anatomical changes associated with flowering; F. W. Went on thermoperiodicity; A. Lang on the genetics of photoperiodism; and there is a brief but inadequate outline by E. Bünning of his fascinating theory of endogenous rhythms. It is a pity that F. G. Gregory was not persuaded to write on vernalization, and R. Harder on his work on *Kalanchoe*. The book maintains a high standard of accuracy.

E. ASHBY

ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

VOLUME VIII JULY 1949 NUMBER 31

Alum: Medium of history

History has been written from many angles—military, political, economic, commercial, ethical, and so forth—and one might well doubt the possibility of discovering a new approach. Yet though the main threads of the vivid and complex tapestry may have been well and truly traced, the tortuous course of a minor thread may reveal points of interconnection previously overlooked. Mr Derek Spence suspected that the story of alum through the ages might prove to be such a thread, and the doyen of historians of science, Professor Charles Singer, has remarkably vindicated him. In a sumptuous volume recently published[1] Singer has in effect worked his way from ancient Egypt to the modern world by following alum as his Ariadne's clue, and has described his journey in a narrative which provides something entirely novel in the sphere of chemical history—and of history in general. There are innumerable histories of chemistry, of various branches of chemistry, and of metals and minerals, but a folio on the history of a single chemical is something to demand and deserve wide attention: for there are many other minor threads, which, in sum, form much of the colour and much of the strength of the fabric of civilization.

Alum was a fortunate choice for this first experiment in a new approach to chemical history. It is a chemical substance with a past—and the past stretches back to the remote days of the Pharaohs. It is also the only substance, apart from certain metals and gems, that has been obtainable from the earliest times in a state of comparative purity. Further, its main uses—as a mordant, as a styptic, and for the treatment of leather—have remained constant throughout millennia. The thread is thin, but strong and continuous.

[1] *The Earliest Chemical Industry*, by Charles Singer, with a preface by Derek Spence. Pp. xx + 338, with numerous illustrations and coloured plates. The Folio Society, London, 1948. Limited editions, 25 guineas and 10 guineas.

The ancient Egyptians, an ingenious and enterprising race, are credited with having built the first ocean-going ships, with which they carried on a flourishing export trade, not only in such sophisticated articles as artificial pearls but in commoner commodities, including alum. They knew how to purify alum, for impurities render it useless as a mordant for bright colours, and a fragment of leather taken from an Egyptian tomb of about 2000 B.C. probably owes its red colour to madder mordanted with alum.

The Assyrians were similarly well acquainted with alum, which they obtained from several localities (Shap Ma'den, Tuz Khurmati, Hamairan, etc.) and used not only as a styptic and for dyeing wool, but for various medical purposes and for tanning. Whether they knew its fire-proofing properties is uncertain, but this particular application of alum was familiar to Aulus Gellius (second century A.D.), who described how one of Mithridates' generals fire-proofed a wooden tower with alum in the war with Rome in 87 B.C. It is possible that alum had been used for fire-proofing some centuries earlier, for when the old temple at Delphi was destroyed by fire, and a new one was to be built, the authorities obtained a gift of 1,000 talents of alum from Amasis, the last native Pharaoh (570–525 B.C.). As Singer observes, the mere carriage of so much alum over seas involved considerable shipping activity, and in fact the whole early history of the alum trade and that of shipping and sea ways are linked together.

In the days of Imperial Rome, alum became a state monopoly in Egypt, and its taxable nature was widely recognized; in A.D. 229 one Aurelius Macrobius is formally described as 'lessee of the alum administration.' The main source of alum was the 'Little Oasis,' 180 miles south-east from Cairo, and the mineral was thence carried to Behnesa, a port on the Nile. From Behnesa it was shipped downstream for local use or for export

from Alexandria. There are references to the alum monopoly in the celebrated Oxyrhyncus Papyri, a touch of humour being provided by the entry concerning a certain camel-driver who claimed, and obtained, repayment of a toll unjustly exacted from him by some officials of the monopoly.

Through the Dark Ages, when applied chemical knowledge was preserved for the most part by obscure craftsmen, familiarity with alum and its properties was maintained, and the alchemists of Islam observed its resemblance to the vitriols. It next comes into prominence, however, in the thirteenth century, when the elusive Geber mentions it in the first clear account of the preparation of nitric acid and *aqua regia*: 'Take of vitriol of copper one pound, of salpeter ½ pound, of Yemen alum ¼ pound. Extract the water with an alembic at dull red heat. The distillate becomes much more active if you add a quarter pound of *sal ammoniacum*, for the liquid then dissolves gold, sulphur, and silver.' Nitric acid, a substance indispensable to the modern world, thus first appeared upon the chemical scene as a product of alum.

By the fifteenth century the preparation of alum had reached manufacturing dimensions, and a conventional 'alum cauldron' was in use which could be worked continuously. It consisted of riveted copper strips with a cast bronze bottom, and was mounted in stone or brick work and heated by a furnace. The alum-stone or alunite was roasted and weathered, and was then added to boiling water in the cauldron. After about half an hour's continuous stirring with wooden ladles the solid matter was ladled out and a fresh supply added. The process was repeated until the solution was saturated; the liquid was then run off to crystallize for about a week and the mother-liquor was returned to the cauldron. Many of these cauldrons were in use in the alum works at Phocaea (Ionia), owned by the Genoese brothers Zaccaria from about 1275 to 1308. The business seems to have been very profitable, for one of the brothers, Benedetto, gave large sums of money to further his favourite project, the recovery of the Holy Land from the Saracens. A contemporary chronicler says that there were over 3,000 alum workers at Phocaea, a figure which gives an indication of the importance of the industry. A century or so later, two Florentine traders placed an order at Phocaea for over 1,000 tons of alum.

In 1461, alunite in large quantities was found in papal territory, and the Pope, Pius II, having in Giovanni de Castro a man who was expert in industrial alum production, at once attempted to create a monopoly. Within two or three years the papal production of alum required the services of no fewer than 8,000 workmen. The technical side of the business was managed by a partnership (including de Castro) known as the *Societas Aluminum:* later a contract was signed with the Medici—and the alum trade had begun to find itself interwoven with the general political history of Europe. A century afterwards, English privateers found alum ships rich prizes, for Britain had begun to dye her own fabrics and the price of alum had soared. Pope Leo X protested in vain that a ship carrying 12,000 ducats' worth of papal alum had been seized by an English rover and brought into Falmouth for the benefit of the Duke of Suffolk.

So the fascinating story goes on, showing, as Mr Spence remarks in the preface, surprising and ever more intricate relations. 'In the process of tracing the applications of this simple chemical substance,' he says, 'we have repeatedly been astonished to find the threads of our story involved in many great human movements, political, economic, social, technical, scientific, philosophical, religious, and artistic.' The same complexity would no doubt be found in the history of many other substances: but they still await the wide erudition of a Singer. And to produce so luxurious a volume as the present, future scholars must await munificence comparable to that of Peter Spence and Sons Limited, who met the cost of preparation and publication. Such an example of enlightened patronage is worthy to be followed. Professor Singer has brilliantly conceived an original approach to the study of science and civilization, and has made a notable addition to the achievements of British scholarship.

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Nitrogen metabolism in plants

W. H. PEARSALL

Plants absorb nitrogenous material in comparatively simple form and build it up with carbon compounds into the amino-acids which are the basis of proteins. The mechanism of protein synthesis and breakdown offers innumerable problems to the biochemist, the botanist, and the plant physiologist, and it seems highly likely that the solution of these problems would result in an important integration of many diverse phenomena of plant metabolism.

The building-up and breaking-down of nitrogenous compounds are fundamental parts of the metabolism of plants, because they deal with the production of a group of substances that are the raw materials of living matter—proteins which make up much of the protoplasmic structure; nucleic acid and the nucleotides, associated particularly with the hereditary properties of cells; and pyrrole derivatives, often pigments like chlorophylls, which are an essential part of the metabolic framework. The chemical complexity of these nitrogenous substances is such that it offers to the biochemist innumerable problems, which are of necessity reflected in the material transformations involved in the synthesis and breakdown of the nitrogenous materials. Fascinating as these problems often are, and necessary as their solution is to any proper understanding of the problems of plant nutrition, their interest often draws us away from taking a broad view of the nitrogen metabolism as a whole.

Although the raw material of fact is often the same, the point of view of the botanist or plant physiologist is normally very different from that of the biochemist; in particular it is broader, in that the observer is often more concerned with overall processes and their bearing on the life of plants than with the distinct biochemical mechanisms involved. A morphological or cytological feature is often as important as a chemical one, and each must be fitted into the general picture. The danger here is of over-simplification in the attempt to create a unified picture; it will be ever present in the following pages. I shall attempt to outline what might be described as the biological background of nitrogen metabolism in plants.

PROBLEMS OF PROTEIN SYNTHESIS

When a plant protein is hydrolysed by acid or by enzymes it yields about twenty amino-acids in widely different proportions. One of the problems of the synthesis of proteins is how these varied mixtures of twenty or more amino-acids can be marshalled during synthesis. The evidence seems to be clear that proteins are not random aggregation products of amino-acid condensation, but that the order in which the amino-acids occur in the protein shows constantly recurring features. It is apparent therefore that highly complicated structural difficulties are involved in protein synthesis, and these can be overcome only by supposing that the amino-acids are assembled on an existing and specific structure, such as the protoplasmic protein itself, as a basis. On this basis new material is grafted, as it were, repeating the pattern and maintaining the complexity. Such a process is hardly to be distinguished from growth, and I shall assume that protein synthesis mainly occurs where growth is taking place, or, perhaps preferably, where protoplasmic synthesis is possible.

It is thus natural to examine the data available for the conditions existing in plant growing-points. The development of the new technique of chromatographic identification of amino-acids has made it possible to detect with some certainty the different amino-acids, even in low concentrations. The method has been applied to various plant tissues by Dent, Stepka, and Steward (1947), and by Alsopp (1948). By this means it has been shown that, while mature tissues often contain the great variety of amino-acids expected from protein breakdown, growing tissues commonly contain only a limited selection, of which glutamic acid is most prominent and always present, though aspartic acid often accompanies it. These facts may suggest that the synthesis of proteins in plants is canalized, as it were, through a limited number of amino-acids. On *a priori* structural grounds we might perhaps expect that alanine with glutamic and aspartic acids would represent suitable building stones for many amino-acids. The methods of further elaboration are unknown.

However this may be, it is not at all difficult to show that the hypothesis of the dependence of protein synthesis upon growth is in large part true. It was shown by Sachs in the sixties of the last century that proteins were quantitatively most abundant in the growing tissues of stem and root and in buds, and of course the germination of protein-rich seeds and the production of new protoplasm in the resultant seedlings must involve, first, hydrolysis of proteins, and then the condensation of new protein in the growing seedlings.

It is necessary to suppose that, in most active tissues, protein metabolism in both aspects is going on all the time, and that we are really dealing with substances continuously being broken down and built up, so that at any moment the amount of protein present in a plant organ is the net result of these two opposing tendencies. As a general rule, therefore, in the mature cell or tissue, where large fluctuations in protein content are not usual, the two processes of synthesis and degradation tend to proceed at more or less equal rates.

It is only recently (with the introduction of the isotopic technique) that this idea of the lability of the tissue proteins has been justified. By using as a tracer the isotope N_{15}, supplied to the plants in the form of ammonium salts, it has been shown that the isotopic nitrogen almost immediately appears in the structure of the amino-acids and proteins. Interchange of nitrogen takes place even in the peptide linkages, so that not only must there be continuous removal and replacement of the α-amino nitrogen of the constituent amino-acids, but also a continual opening of the peptide linkages in the protein chain. These have previously always been regarded as the fundamental part of the protein structure and relatively stable. This reconstitution of the protein may amount to as much as 6 per cent. in 12 hours, and it appears to be more rapid in young leaves than in old. There is, however, a second reason for believing that proteins are continually being decomposed and reassembled. It has been necessary to make use of this idea in order to explain how it is that a large part of the carbon dioxide evolved in respiration comes from protein. A modern explanation first put forward by Gregory and Sen (1937), and by Richards (1938), supposes that carbon chains, derived from carbohydrate in the first place, pass through the 'metabolic pool' and emerge as organic acids (α-keto-acids) to be built up with ammonia into amino-acids and proteins. At the same time, amino-acids resulting from protein breakdown are oxidized to yield ammonia, carbon dioxide, and carbon residues which return to the metabolic pool. As long as carbohydrate is in abundance, the synthetic side of this cycle balances the rate of protein decomposition and amino-acid oxidation, so that little or no change in gross protein content ensues. Nevertheless, using this conception, it is possible to understand how it is that, in the detailed examples studied, respiration rate is mainly dependent on the protein content of the tissue and on the amount of protein synthesis. When the effects of these two factors can be eliminated, there are left certain subsidiary variations associated with the amino-acid and sugar content of the tissues. These also fit in with the general hypothesis.

PHYSIOLOGICAL DRIFTS

In organs such as leaves, the idea of a continual building-up and breaking-down of protein must not only be coupled with the theory of resultant respiratory changes but must also be viewed against a background of continually changing physiological states. The reaction system—protein ⇌ amino-acid—trends towards the left at first, but drifts towards the right as the tissue ages. One of the simplest ways of showing this is by considering the proportion of protein nitrogen present in a tissue such as a leaf at different stages of its existence. This follows a course like that shown in figure 1 for the Swiss Chard (*Beta vulgaris* var. *cicla*), which is amplified from some earlier published work (Pearsall, 1931). The percentage of protein nitrogen is high at first, and falls rapidly to a lower level as the leaf matures, after which it declines much more slowly. When the leaf becomes old, however, there sets in a second rapid decline in protein content, which is finally accompanied by the yellowing of the leaf and, a little later, by its death. Thus there is all through the life of the leaf a slow 'physiological drift,' proceeding at varying rates but resulting in an increased tendency towards protein hydrolysis. For practical purposes, however, we can regard the period of maturity as a steady state in which, as we have seen, the building-up and breaking-down processes are going on at almost the same rate. During the continuation of this steady state it appears (Gouwentak, 1929) that an important factor determining whether protein synthesis ensues in a leaf is whether or not the leaves can gain nitrogen from the roots or from other parts of the plant.

The drifts in physiological condition during the development of the tissue are associated with two other very striking changes in leaf metabolism. In

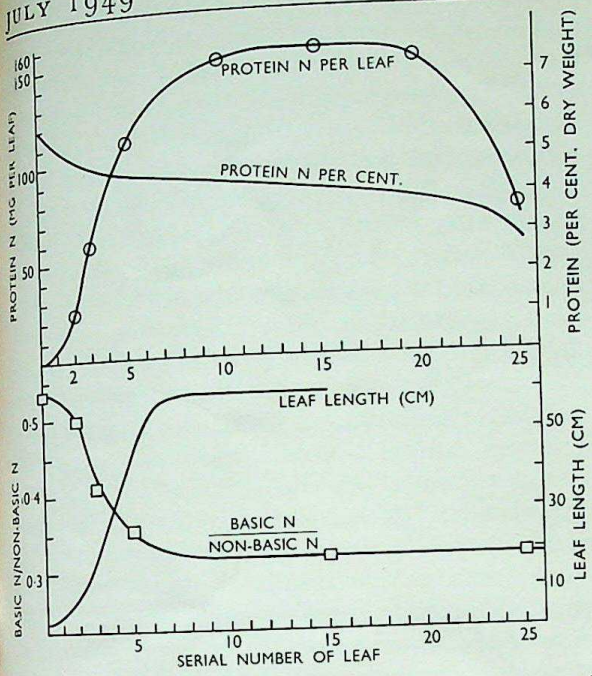

FIGURE 1 – *Protein nitrogen as mg per leaf and per cent. of the dry weight in Swiss Chard* (Beta vulgaris *var.* cicla), *with (below) comparable figures for leaf length and for the ratio of basic N to non-basic N in the leaf proteins.*

the earliest stages of leaf growth, when cell division is most rapid, a very considerable part of the nitrogen metabolism is concerned with the production of the nuclear material (e.g. nucleic acid). Very little attention has been directed towards this aspect of leaf metabolism, but it can be shown plainly enough by observing the change in the ratio of basic nitrogen to other nitrogen liberated from the leaf proteins after their breakdown by acid hydrolysis. This is usually brought about by boiling the leaf material with 6N-hydrochloric acid for 24 hours, resulting in the complete hydrolysis of the proteins. The fall in the proportion of basic nitrogen which results as nuclear division slows down is well shown in figure 1 for Swiss Chard, and it is known that a similar change in the proportion of basic nitrogen is observed in the soluble compounds present in very young leaves. It is evident that the rate of protein synthesis is extremely high during and immediately after the stage of nuclear division (see figure 1), but this matter has been directly studied only in bacteria, in which, using spectrographic methods, Caspersson has shown that there is a correlation between the rates of formation of nucleotides and of protein.

A second change in leaf metabolism follows when cell extension is becoming well marked. The metabolism of the leaf changes over from one which is mainly concerned with nitrogenous substances—proteins and nucleotides—to become a form of metabolism principally concerned with carbohydrates, at first those of the cell walls and glycosides, but subsequently also those formed in green tissues by photosynthesis. In fact, the same type of change may be observed microscopically in the development of the single cell, as it passes from the dividing stage in the meristem with a very thin wall, a large nucleus, and dense protein-staining contents, to the elongating cell, rapidly developing a thicker and more differentiated cell wall, and believed to have a smaller ratio of nucleus to cytoplasm. Similar changes develop during the growth of an algal population (e.g. *Chlorella*). The period of rapid cell-division or exponential growth is one of protein synthesis, and evidently of nuclear synthesis also. As growth slows down, the cells increase in size, and carbohydrate accumulation becomes prominent. Still later, as the cells age, hydrolysis ensues both in the reserve carbohydrate and in protein, so that a considerable proportion of the materials present in the cells may finally escape to the surrounding

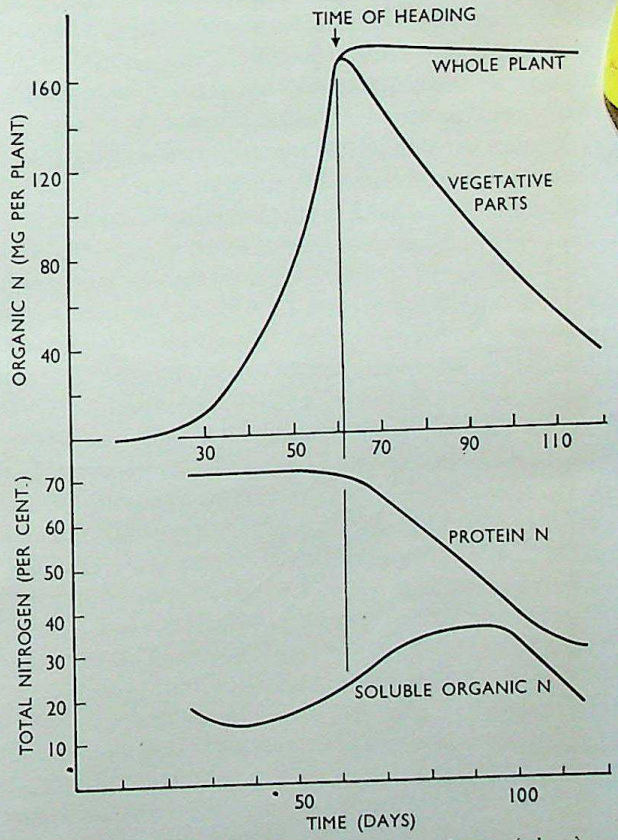

FIGURE 2 – *Organic nitrogen in wheat plants: (above) as mg per plant at different dates, showing the loss of nitrogen from the vegetative parts; (below) percentages of protein and of soluble organic nitrogen in the vegetative parts.*

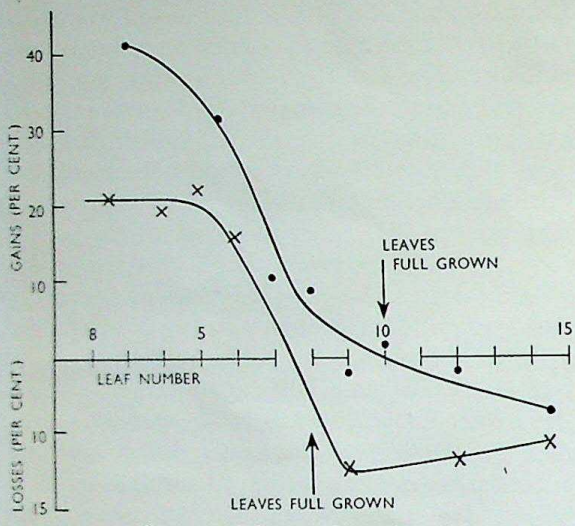

FIGURE 3 – *Gains and losses of protein nitrogen as per cent. of that originally present (after floating on sugar nitrate solutions for three days) in leaves of different ages numbered from the shoot apex downwards. Garden nasturtium* (Tropaeolum majus) (•) *and broad bean* (Vicia faba) (×)

medium. Generally speaking, then, we may say that there is a gradual fall in percentage protein content during the life of a tissue, which is associated not only with the drift in the plant tissues from protein synthesis towards protein hydrolysis, but with a decline in the proportion of nitrogen-rich proteins, and with the replacement of protein formation by carbohydrate accumulation.

These slowly drifting physiological states in an organ such as a leaf are, however, often disturbed in the entire plant by the development elsewhere of actively growing tissues. When this happens, as for example in the development of wheat grains on the plants, hydrolysis of protein in the vegetative parts becomes pronounced, and, as figure 2 shows, most of the protein nitrogen is removed from the vegetative parts to the developing grains. It has been suggested that the balance between protein synthesis in different parts of a plant is determined by the intensity of growth in various places, so that the most actively growing parts behave as 'sinks' into which soluble forms of nitrogen are attracted. Undoubtedly this is not the complete truth. In the primary leaves of the runner bean (*Phaseolus*) at the time of the steady state, the development of the adjacent stem growing-point is associated in the primary leaves with marked increases in soluble nitrogen and a reduction of protein nitrogen. In the leaves, therefore, the balance between protein synthesis and protein hydrolysis is disturbed in the direction of hydrolysis. This type of change in wheat leaves is well illustrated in figure 2, where increases in the soluble nitrogen occur at the time of seed development. Presumably a chemical messenger or some other regulator is transmitted from the newly active growing-point to the vegetative tissue, there to increase the rate of hydrolysis.

It seems also that the steady state in a leaf is disturbed by removing the leaf from the plant,

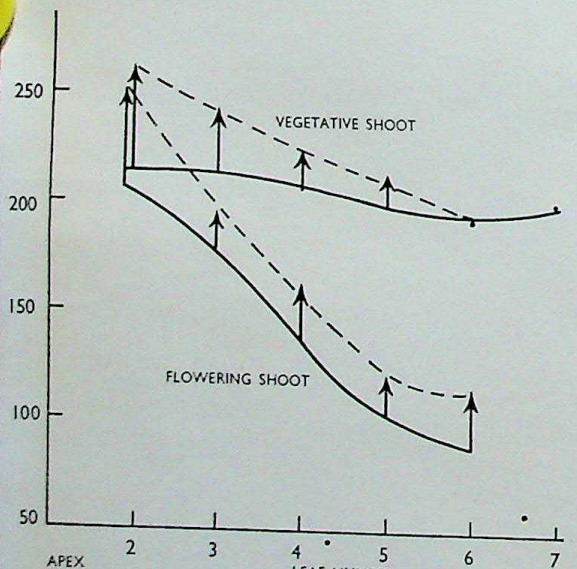

FIGURE 4 – *Protein N (mg per 100 gm fresh weight) in leaves of* Coleus sp. *during vegetative and flowering phases (continuous lines), and increase in protein N in detached leaves floating on sugar nitrate solutions (amount shown by arrows).*

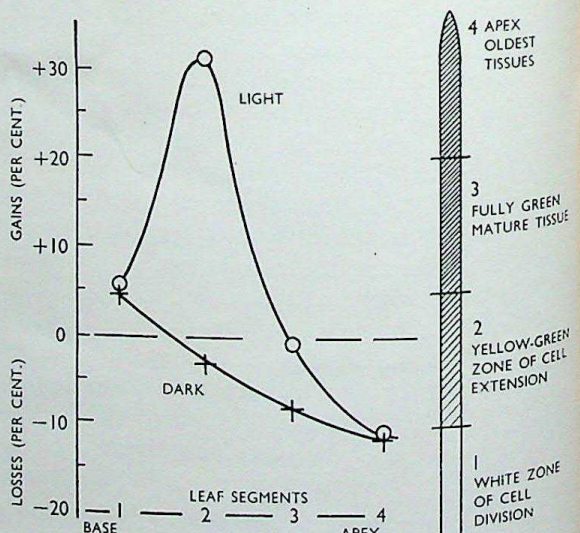

FIGURE 5 – *Percentage gains or losses of protein N by daffodil leaf segments after 72 hours in light (O) and in darkness (+) on sugar-nitrate solutions. The method of dividing leaves is shown on the right.*

for then also there becomes evident a strong tendency towards protein hydrolysis. It is accordingly interesting to determine the conditions under which synthesis of protein can be induced in such isolated tissues. It was shown long ago by Zaleski that a certain amount of protein synthesis resulted when detached leaves were floated on solutions containing nitrate and suitable sugars. Such experiments show clearly that the presence of abundant carbohydrate supplies is necessary for protein synthesis in such a case. From what we have already seen as to the change from growing synthetic tissues to senescent tissues, it should be clear also that the age of the detached leaf is a very important factor in deciding to what extent it can synthesize protein or not. By floating leaves of various ages and sizes on sugar solutions (3 per cent. glucose with 0·2 per cent. ammonium nitrate present) it can be shown that detached leaves from a plant such as the garden nasturtium (*Tropaeolum majus*) are not capable of increasing the net protein content under these experimental conditions after they have reached their full length (figure 3). It is probable that when leaves are attached to the plant they may continue to manufacture protein for a somewhat longer time. Figure 1, for Swiss Chard, shows that overall increase in protein nitrogen can be observed to continue after the increase in leaf length has ceased, and, on our hypothesis of the circulation of material through the cell proteins, it seems that synthesis must continue, and must equal protein breakdown, for a much longer time than is suggested by experiments on detached leaves.

Thus, even in detached leaves, protein synthesis is not always impossible in older specimens. When a plant starts to flower it is often the case, and perhaps invariably so, that the protein nitrogen content of the leaf falls to a very low level. When leaves from flowering shoots of *Coleus* were in this condition of low protein content it was found that they were able to synthesize protein when floated on sugar solution with nitrate present, even although vegetative leaves of corresponding age had lost the capacity to do so. In such an example the flowering shoots had a protein content of only about one-half that of the normal shoots (figure 4) and it looks as though the drain on the protein content had been so great that the leaves had regained the ability to reconstitute the transported material.

In some cases the leaf cannot so easily be used as an age-unit as it is in the above examples. A typical monocotyledonous leaf like that of daffodil (*Narcissus*) consists of tissues of very different ages and potentialities. The tip is the oldest part, and at the base there remains for a long time a white meristematic tissue which continues to grow and to produce new leaf material. To some extent this growing region imposes a barrier between the older parts of the leaf and the rest of the plant, and it is only when the whole leaf is old and showing marked signs of degeneration at its tip that migration of materials from the leaf to the rest of the plant is easily possible. The protein content of monocotyledonous leaves thus continues to increase for a very much longer period than is usual in a typical dicotyledon. The distribution of protein synthesis in such a leaf is therefore complicated by the growth organization of the tissues as a whole. Leaves like those of the daffodil (figure 5), however, are very suitable for investigation, because the leaf can be divided into segments of different ages, starting from the white growing tissue at the base (1) and passing through successive stages. Next come the yellow-green extending tissues (2) just above the base; the middle of the leaf is mature (3) and no longer growing; and the tip is old (4) and may even show signs of senescence.

The overall drifts in the nitrogen content of these different regions are shown in table I, which also shows the drift in nitrogen content of the entire leaves in relation to flower development. The influence of flowering upon the removal of protein is very evident, particularly of course in the apical segments. The data in the last column show that the average protein content of the leaves remains high for a considerable time—actually about twenty days, for the intervals between the four samples were ten days each.

Leaf segments like those of daffodil are a convenient material for studying other aspects of nitrogen metabolism, particularly some of the effects of light. When parallel samples of leaf segments are kept in darkness and in light, floating upon sugar-nitrate solutions, it is possible to show that there are very striking differences in the extent to which the protein synthesis is affected in different parts of the leaf. A typical set of results is summarized in figure 5. This shows that light has no apparent effect upon protein synthesis in the white growing parts of these leaves, but a very great one in the young extending portions, in which there is so large an acceleration of protein synthesis as to cause considerable net gain of protein. These tissues still retain some of their capacity for growth (like the white basal segments), but they also contain a light-absorbing mechanism, the green chlorophyll pigments, and

TABLE I

Protein nitrogen content of leaf segments of daffodil leaves (Narcissus pseudo-narcissus) *as mg per* 10 *gm fresh leaf.*

Stage of development	*Nitrogen content:*				
	of segments				*of whole leaf*
	1 (*base*)	2	3	4 (*tip*)	
(*a*) Young (three-quarter grown) ..	28	37	57	76	51
(*b*) Mature (non-flowering)	27	36	58	74	50
(*c*) Mature (flower buds half grown) ..	28	37	55	67	50
(*d*) Old (flowers in bloom)	24	33	50	52[1]	40

[1] Tips showing beginnings of yellowing.

it is evidently the energy so absorbed that leads to increased protein synthesis. Under the experimental conditions employed, however, the effects of light are insufficient to cause net protein synthesis in mature leaf segments, although light prevents hydrolysis. In the aged tips of the leaves, light does not prevent protein hydrolysis even in the isolated leaf segments.

It is possible in this type of experiment to construct detailed balance-sheets of the materials present in the tissues and in the external solutions. By this method of accounting it can be shown that in the green tissues, as contrasted with the white basal parts, light accelerates both the rate of absorption of nitrate from the external medium and also the rate at which it is utilized (i.e. converted to other things) in the tissues. By making certain assumptions as to what is happening in such tissues, provisional estimates of the rate of formation of organic nitrogenous substances in light and in darkness have been made, which suggest that light accelerates the formation of these substances in green tissues (Pearsall and Billimoria, 1939).

Essentially similar results have been obtained with the green unicellular alga *Chlorella*, growing on a sugar-nitrate medium. In this case it is possible to show that cell-division or protein synthesis (both being equivalent) is so affected by light at 23° C as to give a doubling of the initial cell number or protein weight in fourteen hours instead of in twenty-four. A comparatively small light intensity (100 millimetre candles) will produce this effect during the 'unlimited' or exponential phase of growth in which protein synthesis is most rapid, and little further effect at this stage is obtained by increasing the light intensity.

Analysis of this example, and of the last one (*Narcissus*), suggests that light is effective in two ways—first by increasing the permeability of the protoplasm so that metabolic processes in general go on more rapidly, while substances are absorbed more readily from the external solution. Secondly, however, there must also be a direct effect of light energy, which is used directly in the processes leading up to protein synthesis, as well as in producing sugars which are indirectly effective in giving the carbon chains required for amino-acid formation. This direct effect of light energy seems to act at two stages in the sequence of events leading to protein formation: the stage when nitrate is reduced to ammonia (or its *in vivo* equivalent), and the stage when the substance formed is combined with a carbon chain to give amino-acid or its equivalent.

Very interesting evidence of this direct effect of light on nitrogen metabolism has been obtained by Burström (1943) as the result of studies on wheat plants. He used for experiments wheat leaves previously grown in such a manner that they contained adequate supplies of nitrate. The samples of detached leaves were then illuminated in a stream of air containing the normal concentration of carbon dioxide. Three estimates were made in each experiment: (*a*) the amount of sugars formed in the leaves, (*b*) the amount of nitrate disappearing in the course of the experiment, (*c*) the amount of carbon dioxide absorbed. Burström claims, on the earlier evidence of Nurmia, that during carbon dioxide assimilation, for periods up to twenty-four hours, no carbohydrates other than soluble sugars are formed in the wheat leaves. As he found that the amount of carbon dioxide assimilated in his experiments was considerably in excess of the sugars appearing in the tissues, he was led to assume that the excess of assimilated material not accounted for represented the nitrogenous compounds formed from the combination of products of nitrate assimilation and of carbon dioxide assimilation. A typical set of results is given in table II, which shows how the other assimilates rise as the assimilated nitrate increases and also as the light intensity is raised.

Another point made by Burström is that there seems to be a definite quantitative relationship between the amount of assimilated nitrate and the carbon dioxide assimilation linked with it. The curves illustrating the assimilation of nitrate and the formation of other assimilates follow each

TABLE II

Influence of light on the assimilation during twenty-four hours of carbon dioxide and nitrate, with normal carbon dioxide content of the air. Carbon dioxide and assimilates computed as hexoses. All data as millimols per gm fresh weight of lamina. (After Burström.)

Light intensity (lux)	Increase within the plant of:			
	CO_2 assimilated (a)	sugars (b)	other assimilates (a–b)	nitrate assimilated
0 ..	−0·042	−0·038	−0·004	−0·001
2,900 ..	0·004	0·010	0·014	0·007
8,800 ..	0·057	0·012	0·045	0·019
18,000 ..	0·174	0·098	0·076	0·031
30,000 ..	0·303	0·098	0·127	0·040

other closely, and indicate that, for each molecule of nitrogen reduced, about fourteen molecules of carbon dioxide are combined with it into materials of a non-sugar nature. Now, of course, there is no protein which has a molecular relation of C : N in any way resembling this value of 14. The only common plant material which has a C : N relation of this sort is the green pigment chlorophyll (C : N = 13·6). As a general rule, the C : N ratio of protein is close to 3·9, so that, assuming that Burström's interpretations are correct, there must be formed, in addition to protein, some other carbon-rich substance. If the tissues were growing, this might be cell-wall material, e.g. cellulose, which would not appear in the carbohydrate analyses. There is, however, another possibility, which is that the plants form organic acids in addition to protein during the assimilation of nitrate. In the experiments with *Narcissus* already mentioned, it was found that light produced little or no alteration in internal sugar concentration as compared with darkness. This indeed might be expected, since the leaf segments were floating upon sugar solution and both the illuminated and the darkened segments took in much sugar. In contrast, however, there were marked changes in acid content, though this was measured only as the titratable acidity. The acidity was much higher when the leaf segments were illuminated, a condition in which they also converted much more nitrate. The extra acid production was roughly in proportion to the larger nitrate assimilation.

More definite evidence of a connection between nitrate assimilation and acid production has since been obtained from another species of *Narcissus* (*N. poeticus*), and also from tobacco and *Bryophyllum* plants, by Vickery and Pucher (1940) and their associates. They have examined the effects on these plants of supplying them during growth with nitrates, rather than with ammonium salts, as a source of nitrogen. They find that one well-marked metabolic effect of this treatment is that larger quantities of organic acids appear in the tissues. Particularly prominent are the increases in malic acid and isomers of citric acid, in addition to other acids as yet unidentified. We thus have to suppose that nitrate assimilation is linked to organic acid production in such a way that each unit of nitrogen assimilated leads to an increase in the amount of carbon compounds entering the organic acid pool. It may be pointed out that this increase must be considerable, although the data do not enable a quantitative estimate of the magnitude to be made. It must allow not only for the increased acid content of the tissues, but evidently also for those carbon chains necessary to build up amino-acids from the products of nitrate assimilation. Thus, if Burström's figure of 14C : 1N be accepted, and if about four carbon atoms on an average might represent the proportion of carbon chains required for protein, the remaining ten carbon atoms would be those going to other metabolic products, such as organic acids and cell-wall materials.

Even in its earlier stages, then, nitrogen assimilation serves to link widely different aspects of metabolism. The evidence here surveyed suggests that we shall ultimately find that a knowledge of the physiology of protein synthesis and degradation will provide an important means of integrating many phenomena of plant metabolism.

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The Lister Institute of Preventive Medicine

HARRIETTE CHICK

Early in 1889, the Lord Mayor of London, Sir James Whitehead, went to Paris to consult Pasteur about the control of rabies. He returned with the determination to establish a treatment centre for rabies in London. In spite of opposition he drove on with his project, and the British Institute of Preventive Medicine was founded in 1891. Dr Chick tells the story of the institute (now the Lister Institute) and describes some of its manifold activities.

Although the Lister Institute under its present name and organization has been actively engaged for over forty years in research in medical and allied sciences, its activities have in reality been spread over more than fifty years. As the British Institute of Preventive Medicine, it owed its origin in 1891 to the energies of a committee formed after a Mansion House meeting held two years earlier to discuss the urgent problem of the control of hydrophobia in Great Britain. The successful treatment of the disease at the Pasteur Institute in Paris, where over 200 of our fellow-countrymen had been treated gratuitously, was made the basis of an appeal for funds to discharge this debt, and as a result a sum of about £2,000 was sent to Pasteur as a contribution to his recently opened institute. At the same time the committee, recognizing the seriousness of the lack of any institute in this country having aims similar to those of the French or other Continental institutes, launched a further appeal for funds to remedy this national defect.

Financial support was forthcoming from several City Companies and other sources, and the British Institute of Preventive Medicine, which had been amalgamated with the then existing College of State Medicine, became possessed of a capital sum of about £50,000 and of premises in Great Russell Street, London. Here the work of the new institute was started. By the beginning of the present century, however, changes had taken place in its name, its system of management, and its places of work. The Lister Institute of Preventive Medicine became established in buildings on a fine site on the Chelsea Embankment which had been purchased under very generous terms from the then Duke of Westminster. Lord Lister, first chairman of the governing body, held the office until ill health compelled his resignation in 1904, after which date he became the president of the institute; he was succeeded as chairman by Sir Henry Roscoe. The latter was in turn succeeded by Sir John Bradford, Sir David Bruce, Professor William Bulloch, and, in 1942, by Sir Henry Dale.

While the energies of the staff and other workers in the Chelsea buildings were mainly devoted to fundamental research in medical science, an important part of the work of the institute was connected with the experimental farm for the study and production of diphtheria antitoxin and other therapeutic sera. In the first instance, in the absence of special accommodation, horses for this purpose were housed at the Brown Institution in London through the co-operation of Dr (later Sir Charles) Sherrington, who was then the professor superintendent. There, in August 1894, the first diphtheria antitoxin to be produced in this country was obtained by Dr M. Armand Ruffer (at that time Director of the Institute), and by Sherrington. In the same year this branch of the institute's work was transferred to premises at Sudbury, Middlesex, and in 1903 to more suitable quarters in open country at Elstree, Hertfordshire.

ORGANIZATION OF THE SCIENTIFIC ACTIVITIES OF THE INSTITUTE

The appointment of Dr (later Sir Charles) Martin, F.R.S., in 1903 as director was followed by expansion of the institute's activities in many directions.

The number and character of the different departments of the institute has been kept fluid and elastic. Against a permanent background formed by the main departments of bacteriology, experimental pathology, and biochemistry, other smaller divisions have from time to time arisen, flourished, and in turn diminished. These have usually been formed in response to need for special

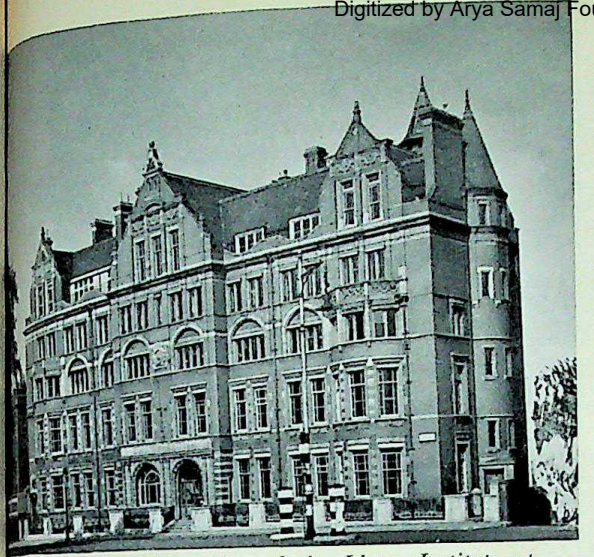


FIGURE 1 – *The laboratories of the Lister Institute at Chelsea, London.*

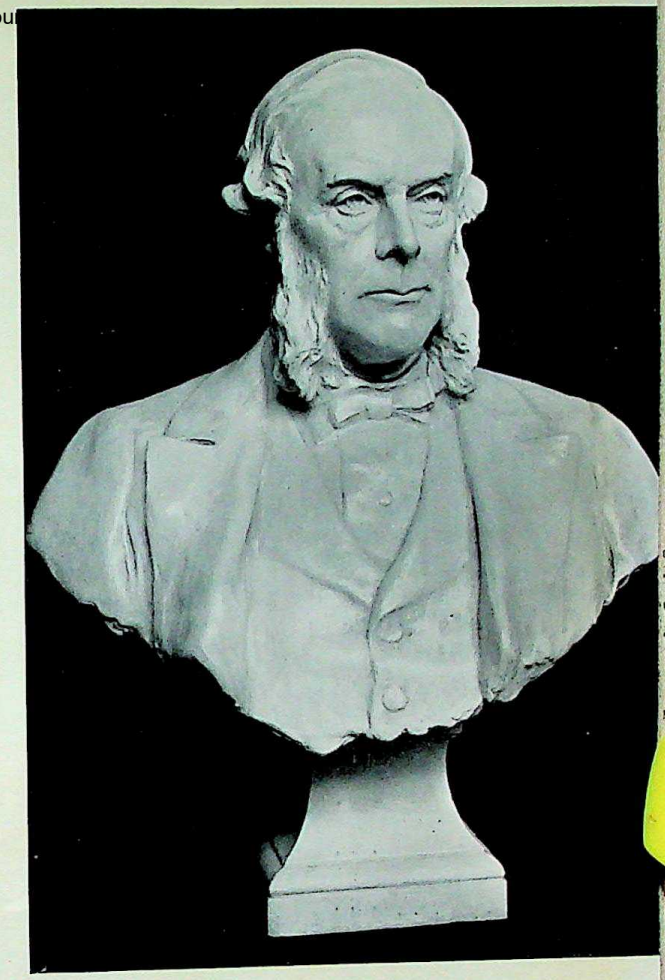


FIGURE 2 – *Lord Lister. Original plaster cast from a bust by Sir Thomas Brock. (National Portrait Gallery.)*

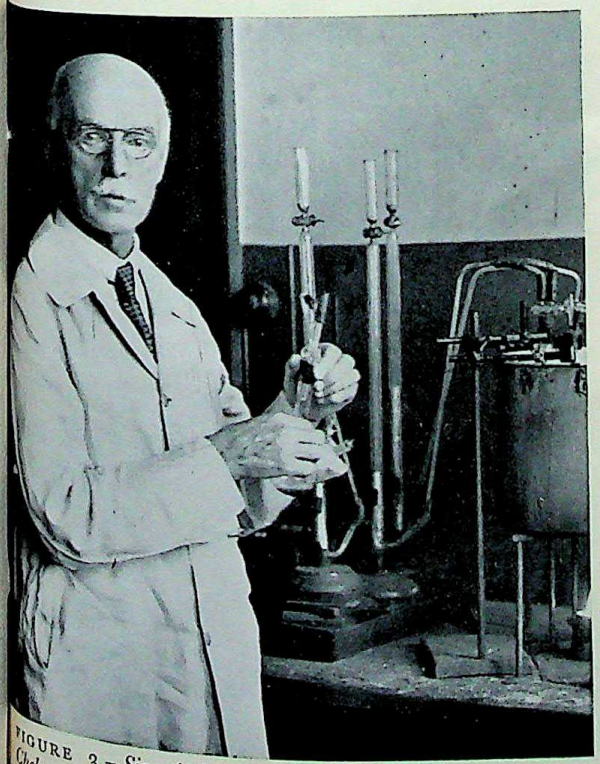


FIGURE 3 – *Sir Arthur Harden in his laboratory at Chelsea, 1929.*

FIGURE 4 – *Sir Charles (then Lt.-Col.) Martin in his laboratory in Cairo, 1916.*

FIGURE 5 – *The laboratories of the Lister Institute at Elstree, Hertfordshire. On the left are the buildings for the preparation of vaccine lymph and bacterial vaccines; those in the centre are for the preparation of antisera. The stables and farm buildings are seen on the right.*

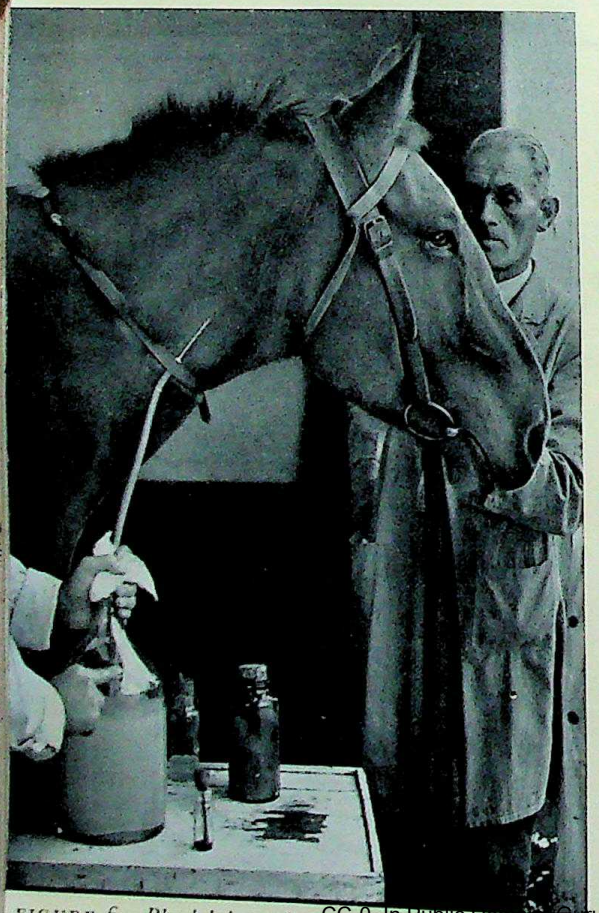


FIGURE 6 – *Blood being taken, with aseptic precautions, from the external jugular vein of an immunised horse. The*

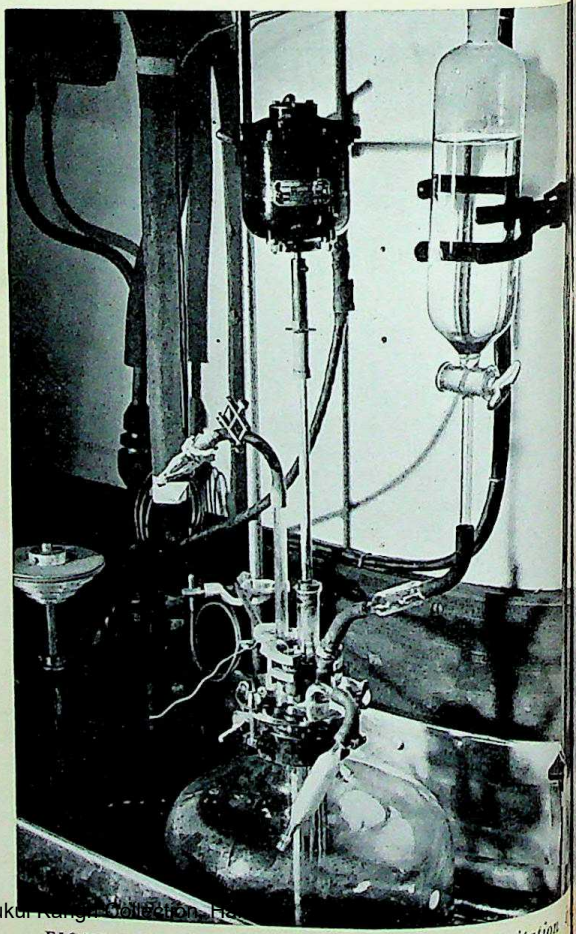


FIGURE 7 – *Apparatus for the aseptic precipitation ether of gamma globulin from human serum.*

research of a topical character, and sometimes to provide scope for the special gifts of individual members of the staff. Among such have been the departments of protozoology, entomology, and statistics. The study of accessory food factors, begun in 1911 and extended during the years of the 1914–18 war in response to wartime needs, led to the formation in due course of a Division of Nutrition. The National Collection of Type Cultures was founded in 1920 by the Medical Research Council and housed since that date in the Lister Institute. It developed from a relatively small set of authentic tested cultures of pathogenic organisms used for teaching, research, and the preparation of the diagnostic sera which were distributed to the pathological services of British forces during the 1914–18 war. The most recently formed unit, that of biophysics, originated from the gift in 1935 of an ultracentrifuge by the Rockefeller Foundation.

It has been the custom to maintain a relatively small scientific staff which, together with the holders of the various research fellowships and scholarships included in the establishment, has never exceeded about thirty in number. The hospitality of the institute and its resources have, however, always been made available to suitably qualified guests who may wish to carry out investigations in the fields covered by the institute's activities. The number of such attached workers, including British investigators and others from the Commonwealth and from foreign countries, has at times nearly equalled that of the established staff. In particular, many members of the external scientific staff of the Medical Research Council, as well as workers holding temporary grants or research fellowships from that body, have been accommodated, and one or more holders of Beit Memorial research fellowships have usually been found among the attached workers at the institute.

SOME OUTSTANDING RESEARCHES

SPREAD OF PLAGUE

The institute took an active part in the elaborate series of investigations on the spread of plague organized in 1905–8 by the committee for the investigation of plague in India, on which body the institute was represented in addition to the Royal Society and the India Office. In 1905 the director, Dr Martin, with two members of the staff, went to India to work in the Parel Laboratory, Bombay, where, in collaboration with members of the Indian Medical Service, an elaborate series of experiments was planned and carried out with the aim of determining the mechanism by which bubonic plague is spread among rats and conveyed to human subjects. These researches, which were continued over three years, succeeded in establishing as the carrier of the plague bacillus, the rat flea, *Xenopsylla cheopis*, which usually infests the wild rat (*Mus rattus*) in tropical and subtropical regions of the world.

CAISSON DISEASE AND THE DANGERS OF DEEP-SEA DIVING

Work on this subject was rendered possible by the gift in 1906 from Dr Ludwig Mond of a large steel pressure chamber fitted with a double-action compressor pump for circulating air at different pressures. The chamber was large enough to accommodate two persons comfortably, and was used for trials on men and animals with compressed and rarefied air. Studies could thus be made upon physiological adaptation to raised and lowered atmospheric pressures, such as are experienced in deep-sea diving and caisson operations.

ALCOHOLIC FERMENTATION

The researches of Dr (afterwards Sir Arthur) Harden and his pupils on the alcoholic fermentation of sugar by yeast are some of the most famous which have emanated from the institute, and have proved to be of unexpected general scientific importance. In this work, the first important achievement was the discovery that yeast juice could transform sugar into alcohol only in the presence of another substance acting as a co-enzyme or co-ferment. This could be separated from the zymase ferment of yeast by passage through a gelatin filter. Neither alone could ferment sugar, but when they were mixed fermentation proceeded at a normal rate. The chemical constitution of the co-ferment, or co-enzyme as it is usually called, was later investigated with success by Professor v. Euler of Stockholm, with whom Sir Arthur shared the Nobel prize for chemistry in 1929. A second fundamental discovery was the fact that before any breakdown of the sugar molecules occurred combination with phosphoric acid was necessary, and that only after this preliminary phosphorylation had been achieved did they become susceptible to disruption by the enzymes in yeast zymase.

These discoveries of Harden and his colleagues, showing the importance of phosphorylation, have provided the clue to the elucidation of many biological phenomena involving the action of enzymes. For example, the mechanism of the

production of lactic acid in metabolism of carbohydrates by the enzymes of muscle has shown an astonishing similarity to that of yeast enzymes in the alcoholic fermentation of sugar.

Further work on carbohydrate-phosphoric esters, carried on by Professor R. Robison, led to the discovery of the hexosemonophosphate which commonly bears his name. Phosphoric esters were found to be concerned in the deposition of calcium phosphate during the ossification of cartilage in growing animals, and thus to play an important part in the formation of bone.

OTHER BIOCHEMICAL RESEARCHES

Since 1940, and following the death of Professor Robison, the activities of the biochemical department have been largely concerned with the isolation and characterization of the substances responsible for the group-specificity of human red blood corpuscles. A knowledge of the physical, chemical, and immunological properties of these substances is essential for a thorough understanding of the scientific basis on which the modern technique of blood transfusion rests. Dr Morgan and his colleagues have succeeded in isolating these specific factors, and have investigated their most important immuno-chemical properties. It is now established that the A, B, and the so-called O specific substances are mucoids, that is, polysaccharide-aminoacid complexes, which possess extremely labile structures. These closely related gene products are very similar chemically, although each possesses its own specific immunological characters.

Studies in the department since 1942 have also included in the role of the toxins of *Clostridium welchii* in gas gangrene infections, and the chemical nature of the bacteriostatic substances gramicidin, gramicidin S, and tyrocidine.

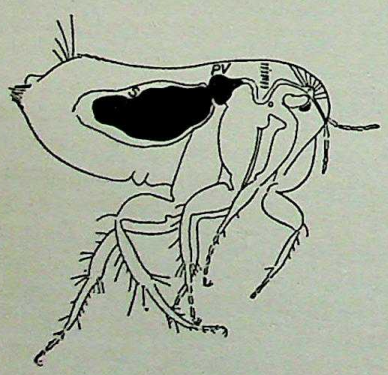


FIGURE 8 – *At the beginning of this century the Lister Institute played an important part in the elucidation of the mechanism of transmission of bubonic plague. This drawing of a plague-infected rat-flea with proventriculus (PV) and stomach (S) blocked with culture of plague bacilli is taken from Bacot and Martin, J. Hyg.* 13, 423, 1914.

BACTERIOLOGICAL INVESTIGATIONS

In the earlier decades of the present century the department of bacteriology was the largest and probably the most active in the institute. Chief among the workers was Dr (later Sir John) Ledingham, F.R.S., who became bacteriologist-in-chief in 1909 and was director of the institute from 1931 to 1943. His work on trench fever, on its minute causal 'rickettsia' forms, and on the technique developed in its study, was a preliminary to important work on the viruses of vaccinia and fowlpox. There is now no doubt that the so-called 'elementary bodies' which could be demonstrated under a high-power microscope represent at least one stage in the life of these viruses. Proof was forthcoming in the results of later work, which showed the specific antigenic action possessed by preparations of these elementary bodies when injected into horses. Other infective viruses which were made the subject of study were those of vaccinia and foot-and-mouth disease.

BACTERIAL VARIATION

Bacterial variation is a subject which engaged the attention of members of the bacteriological staff for many years, particularly of Sir Joseph Arkwright, Sir John Ledingham, and Dr Penfold. The discovery that alteration in the shape of the colonies of many pathogenic bacteria was associated with alteration in virulence and immunizing value was an impetus to these studies and has afforded valuable results.

ROLE OF VITAMINS IN NUTRITION AND ETIOLOGY OF NUTRITIONAL DEFICIENCY DISEASES

As early as 1911 and the years following, Dr Casimir Funk was engaged in the department of biochemistry in an attempt to separate from yeast the substance, to which he gave the name of 'vitamin,' which would prevent tropical beriberi in man, and in birds the polyneuritis already recognized as an analogous disease. At the same time in the department of experimental pathology a study was made of the distribution of this vitamin in common foodstuffs, and of the influence of the amount of carbohydrate in the diet upon its requirement.

During the first world war, occurrence of beri-beri and scurvy among our armies abroad created

a further urgency for the study of these nutrition diseases. Temporary helpers were secured to assist the greatly diminished institute staff, and researches were undertaken upon the properties and distribution in foodstuffs of the anti-beriberi vitamin, now known as vitamin B_1 (aneurin or thiamin), and of the anti-scorbutic vitamin, now known as vitamin C or ascorbic acid.

The prevalence of rickets among children of the countries of central Europe following the privations of the 1914–18 war focused attention upon this disease and upon the unsolved problem of its etiology. Reports from Vienna in 1919 also described a condition of osteomalacia, seen in the poorer elderly population, which was thought to be analogous to that of rickets in children. In the autumn of 1919 Vienna was visited by a small unit of workers, supported jointly by the Lister Institute and by the Medical Research Council, which continued to work in that city for about three years. With the friendly co-operation of Professor Clemens v. Pirquet and his staff at the university *Kinderklinik* an elaborate series of investigations was made upon the etiology of rickets. The results of these trials showed that the disease in infants could be prevented or cured with certainty, either by administration of preformed Vitamin D in cod liver oil or other foods, or by exposure to natural sunshine or to ultra-violet irradiation from artificial sources, and that the physiological action of these three agents was indistinguishable. Hunger osteomalacia in adults and late rickets in adolescents were found to react in a similar manner.

RESEARCHES ON HUMAN BLOOD-PLASMA

By special methods involving the use of ether, the active fractions of blood-plasma—the gamma globulin, the thrombin, and the fibrinogen—can be isolated. The fibrinogen when mixed with thrombin forms a solid clot, and is used in surgery to surround and secure a sutured nerve. By special treatment a sponge-like preparation of 'fibrin-foam' is produced. This, if moistened with thrombin and placed on an area of bleeding, causes the blood to form a solid clot in the sponge, which can be left in position and, being a natural substance, is slowly absorbed by the body and is a form of dressing of special use in brain surgery. The gamma globulin, the fraction which contains the natural antibodies against certain diseases, has been used successfully for prevention of measles or mitigation of its severity. The staff of the unit of biophysics is concerned in the preparation of these materials, and an extensive series of drying plants has been constructed in which they can be dried from the frozen state and supplied in the dry form. In addition, special refrigerated rooms have been erected and methods of preparing human plasma for transfusion purposes have been developed.

NATIONAL SERVICE IN THE TWO WORLD WARS

The nature of the contribution made to national service has differed somewhat in the two world wars. In the years 1914–18 almost the entire staff, both scientific and subordinate, was occupied in service abroad in the pathological and hygienic services of the Royal Army Medical Corps. Only a small remnant, consisting largely of women, remained to cope with the routine and research work of the institute, which assumed a definitely topical character in response to the national needs. In the second world war this island was itself in the front line of the conflict and the staff of the Institute was occupied to a greater extent with national service at home. The vulnerable position of the buildings at Chelsea, which suffered one direct hit during the London air raids in addition to damage from blast on more than one occasion, necessitated the evacuation of several departments to more peaceful surroundings where suitable hospitality was offered and accepted. In such often improvised accommodation research work was continued; investigations of more fundamental nature were laid aside for the time being and others of more direct application to national wartime needs were adopted as far as possible. Among these may be mentioned the investigations on the differing nutritive value of flours derived from different portions of the wheat grain, undertaken to provide information which might guide the authorities in selecting the most economical and nutritious flour for bread-making under war conditions, and the studies of the stability of vitamins in foods under conditions of storage. Considerable progress was also made in the preparation of protective and curative vaccines against typhoid fever and of curative sera for gas gangrene.

Under the guidance of the present Director, Dr A. N. Drury, F.R.S., appointed in 1943, the institute has undergone a considerable degree of reconstruction necessitated by the changed conditions obtaining at the end of the war. Its activities in the future will doubtless differ from those of the past, as befits a research institution where change and development are symptomatic of healthy life and progress.

Decay of timber by fungi

W. P. K. FINDLAY

The role of fungi in causing decay in timber has been recognized for about a century, and much work has been done on the elaboration of methods of wood-preservation. A problem of first importance was the recognition of wood-rotting fungi in the absence of their fructifications: this has been largely solved by making comprehensive culture collections. Dr Findlay shows that modern knowledge renders unnecessary the waste of much good timber.

HISTORICAL IMPORTANCE

When the warships that defended the shores of Great Britain were built entirely of wood, the prevention of rot in their hulls was a matter of supreme importance to the nation. From the time of Charles II, right up to the coming of the ironclads in the middle of the nineteenth century, there are numerous records of the loss and damage to warships caused by rot. Samuel Pepys, the famous diarist who was also Clerk to the Admiralty Commission, reported that ships had been 'suffered to heat and moulder till I have with my own hands gather'd toadstools growing in the most considerable of them, as big as my fists.'

The problem reached its height during the Napoleonic wars, when large numbers of vessels were built of unseasoned timber; great men-of-war, containing 3,000 loads of timber, became useless in two to three years. At the conclusion of hostilities, half the ships in the Navy were said to have been in a rotten state; some were found to have rotted even before they were launched. The subject was frequently raised in Parliament and became a matter of public concern and alarm. Although the role of fungi in causing decay of timber was, as yet, by no means clearly understood, James Sowerby, the eminent botanist, in a report to the Commissioners of the Navy in 1812, described and named the fungi which he found, thus clearly associating the decay of the wood with the presence of the fungi. He was well aware of the importance of providing proper ventilation to prevent accumulation of moisture (see figure 9).

The term 'dry rot' was first used about 1775, to describe the fungal decay which eventually reduces wood to a dry-looking mass that crumbles to powder at a touch. It is in many ways an unfortunate appellation for a trouble that invariably develops under damp conditions, and the term has frequently led to misunderstandings; it has, however, become so well established in the English language that it cannot be altered. Its use should be restricted, however, to the decay of timber in buildings, brought about by certain specialized fungi. Dry rot of timber in buildings does not appear to have become serious until towards the end of the eighteenth century, when soft woods began to replace the much more durable oak for building purposes, and there are many references to dry rot in woodwork of famous buildings about this period. Prizes were offered by the Royal Society of Arts, London, for a cure for dry rot, and many strange specifications and remedies were proposed in articles published in the early nineteenth century.

An important practical advance in the art of preserving wood against decay was made by Bethell, who patented, in 1838, the process of impregnating wood with an antiseptic under pressure—a process subsequently developed and improved by Boulton, whose patent is dated 1879. Although the practical application of this method of preserving wood, by impregnating it with creosote under pressure, was soon taken up on a large scale in this country, little attention to the subject of wood rot was given by scientific men until Marshall Ward began his studies at Coopers Hill in 1890–1900.

To Robert Hartig, in Germany, must be given the credit of first establishing that fungi are the cause of decay in wood, and his work was followed by other scientists in Germany, a country in which forestry and timber problems have for a long time received serious attention.

Pioneer work in the United States of America was undertaken at the beginning of the present century by von Schrenk, and since then the work of the Forest Products Laboratory at Madison in Wisconsin, and other research institutes, has contributed a great deal to our knowledge of wood-rotting fungi.

In the past Great Britain has not been to any

noteworthy extent a timber-producing country, and little research on the diseases of trees or of timber was undertaken until after the first world war. The establishment in 1927 of the Forest Products Research Laboratory at Princes Risborough, having as its objective the better utilization of timber, provided a centre for research on wood-rotting fungi and the preservation of wood.

RECOGNITION OF CAUSES OF DECAY

One of the first problems to be tackled was the development of means of recognizing wood-rotting fungi in the absence of their fructifications. Only a few fungi produce a rot which is sufficiently distinctive to allow the causal fungus to be identified with certainty. Microscopic examination of the hyphae, and of their effects on the cells of the wood, seldom yields any more definite information than that a wood-rotting fungus is at work. It was found, however, that the appearance of the fungi, when grown in pure culture on a standard medium, is often sufficiently characteristic to permit the species to be recognized, either by its texture or colour (see figures 1 and 2), or by the presence of certain microscopic features. Physiological characteristics, such as the rate of growth at various temperatures, reaction to varying degrees of acidity in the medium, etc., can also be helpful in determining the identity of a fungus in culture. In order to become familiar with the characteristics of these fungi in culture it is necessary to have at hand cultures prepared from named fructifications, and a comprehensive collection of such cultures must be available in any laboratory undertaking research in timber pathology. The practical value of being able to identify the cause of decay in any sample of wood is that, once identification of the causal fungus is established, the source and origin of the infection can usually be determined. For instance, if the fungus found responsible for decay in imported rock elm timber of a boat can be identified as a species that occurs in standing elm trees in Canada, it can be concluded with a fair degree of certainty that the wood was infected before shipment, and indeed came from a diseased tree.

It is difficult to describe cultures with sufficient precision to enable another worker to recognize them, but recently attempts have been made to prepare comprehensive keys for the identification of fungi from their appearance in culture on agar media. Figures 1 and 2 illustrate cultures that are sufficiently characteristic to be readily recognized from their general appearance.

EFFECTS OF DECAY ON PROPERTIES OF WOOD

Wood-rotting fungi secrete enzymes that can bring about profound changes in the physical properties and chemical compositions of timber. While it is a matter of common knowledge that rotten wood is soft, it is only recently that accurate tests have been made to discover how far the various strength-properties of wood are affected at different stages of attack by various kinds of wood-rotting fungi.

During the war, when supplies of high-grade timber for aircraft were scarce, it became a matter of importance to determine the influence of various defects and blemishes on the mechanical properties of these woods, so that no unnecessary rejection of timber should be made. It was found that plywood made from veneers containing slight incipient decay might have strength-properties but little inferior to those of plywood made from perfect veneers, and good use was thus made of material that would otherwise have been scrapped.

The property which is most rapidly affected by incipient decay is the toughness or resistance to impact or shock. For instance, in one experiment the toughness of samples of ash (*Fraxinus*) exposed to the fungus *Polyporus hispidus* fell by 20 per cent. after two weeks' exposure to attack, and was reduced by 75 per cent. after only eight weeks. Bending strength was also affected immediately, but depreciated only by 30 per cent. after 28 weeks' exposure. This immediate effect on toughness is probably due to breakage in the linkages between the chains of cellulose molecules, brought about by the hydrolysis caused by the fungal enzymes.

The density of wood falls as fungal decay proceeds, and, in the case of fungi that can attack all its constituents, wood can be utterly consumed. On a study of their chemical action, the fungi that attack wood can be divided into two classes:

1. Those which produce hydrolysing enzymes and attack the cellulose and associated pentosans, bringing about *brown* carbonizing rots which leave the wood in a friable, powdery condition (see figure 3).
2. Those which produce oxidizing as well as hydrolysing enzymes, attack all the constituents of the wood, including the lignin, and bring about *white* or light-coloured rots (see figures 4 and 5).

It is easy to test cultures of wood fungi for the presence of oxidases by the addition to the culture fluid of a substance such as guaiacum, and this reaction is a useful diagnostic feature as to the type of rot a fungus can produce.

NATURAL DURABILITY OF WOOD

Timbers vary greatly in their resistance to fungal decay. Some, like beech and poplar, perish rapidly if left in contact with the ground; others, like teak and ironbark, may last for centuries. There has been a good deal of speculation as to the reason why one timber is more durable than another. Attempts have been made to correlate the durability of timbers with their densities, but this correlation does not hold, for there are some lightweight woods (such as western red cedar) which are very resistant to decay, and some fairly heavy woods which are readily decayed. Reasons for differences in natural resistance have therefore had to be sought in the chemical make-up of the wood. The basic wood substance appears to vary comparatively little from one species to another within the groups of the broad-leaved and coniferous trees, so it is among the minor constituents, such as the water- or alcohol-soluble extractives, that one must seek the natural preservatives which confer resistance on the wood. Recent work in Sweden has shown that it is the presence of small amounts of a highly toxic phenolic compound called pinosylvin which renders the heartwood of Scots pine so much more resistant than the sapwood, while the similar material in western red cedar has been isolated and named thujaplicin. Cartwright has shown that the resistance to decay may vary in different parts of the trunk of a single tree of western red cedar, being lower at the centre of the heartwood than in the outer layers, and that this variation can be correlated with the amount of water-soluble material present.

Laboratory tests have been devised by which the natural resistance to decay of a wood can be determined much more rapidly than in field exposure trials. Many unfamiliar timbers from Africa and South America are now coming on the markets of western Europe to replace well-known species that are scarce, and it is essential to find out as much about their properties as possible, so that they can be put to the best use with the minimum delay.

PRESERVATION OF WOOD BY CHEMICALS

For a hundred years or so, creosote distilled from coal tar has been the standard material for the preservation of timber, and for many purposes no better preservative has been, or is likely to be, found. It has, however, certain disadvantages, such as its effect on paint. In parts of the world remote from industrial areas where tar distillation is carried on, the cost of transport may make creosote expensive, and in these circumstances it is more economical to use a water-soluble material which can be transported in solid form and made up with water on the spot. Until recently, most water-soluble preservatives suffered from the disadvantage that they were leached out of the treated wood by the action of rain, but it has been found that, by the addition of chromates, toxic chemicals such as copper and arsenic can be fixed and rendered less soluble after they have penetrated into the wood, and several effective water-soluble preservatives of this type are now on the British market. A recent development has been the use of substances toxic to fungi which are soluble in oils but insoluble in water, so that the toxin is deposited in an insoluble form after evaporation of the solvent. Pentachlorophenol and copper naphthenate are two compounds now used extensively for the preservation of wood in this way.

The length of time that is required to test wood preservatives by field or service tests has led to the development of rapid laboratory methods for their evaluation, and a British Standard method for determining the toxicity to fungi of wood preservatives has been published.

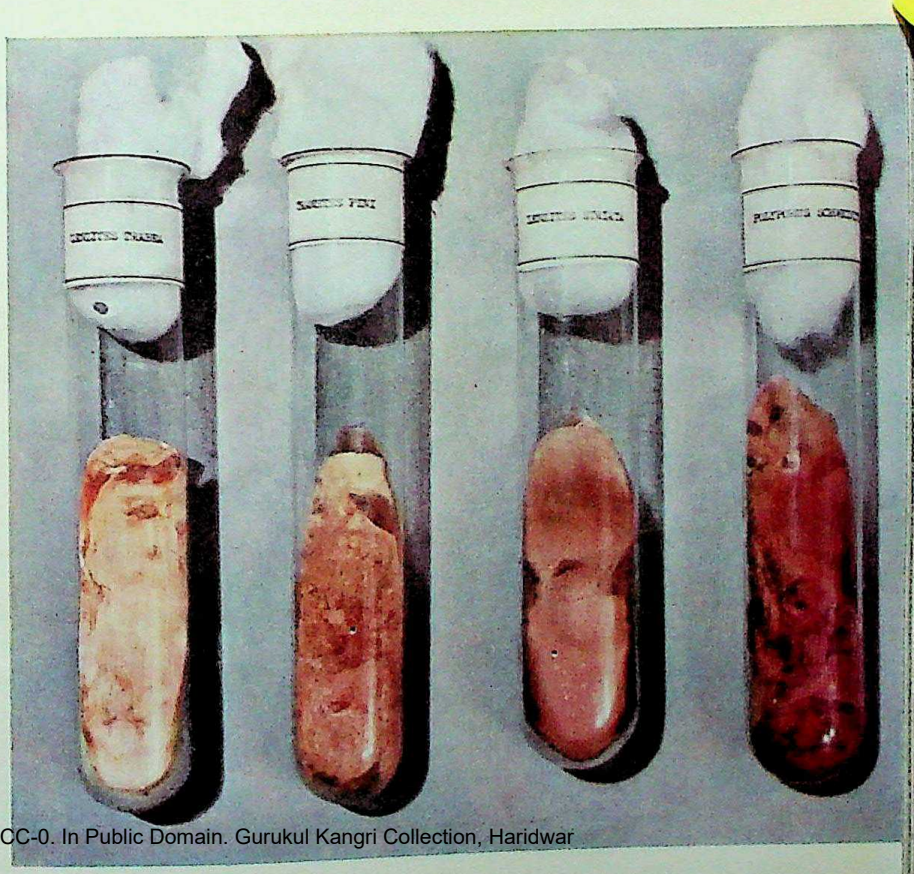
PREVENTION OF DECAY OF TIMBER IN SERVICE

In spite of the advances in knowledge about the physiology of wood-rotting fungi and about means of preventing damage by them, an immense amount of wood is, in the aggregate, allowed to decay prematurely even in highly developed countries. Few countries still possess a superabundance of timber, and none can afford to waste this precious raw material, for which there is an unsatisfied world demand. The cost of effective impregnation with preservatives has not risen to the same extent as the cost of timber (which in Great Britain is three to four times its pre-war figure), and therefore the saving that can be effected by preservative treatment shows a marked increase over the pre-war level.

In Europe, repair and maintenance work on all types of buildings, especially dwelling-houses, was neglected for five years or more, and dry rot is exceedingly prevalent; it is no exaggeration to say that millions of pounds sterling have been spent since the war on repairing the ravages of dry rot in England alone (see figure 13). Dry rot has been particularly prevalent in buildings where fires, caused by incendiary bombs, were extinguished with large volumes of water. Much of the damage

FIGURE 1 – *Cultures on 5 per c malt agar of wood-rotting fungi. S of these possess a characteristic tex or coloration by which they car readily recognized.*

From left to right: Collybia v tipes (*with fructifications*), Meru lacrimans, Polystictus sanguin *and* Stereum rugosum.



RE 2 – *Cultures on 5 per cent. agar of (from left to right):* zites trabea, Trametes pini, zites striata, Polyporus schwei-

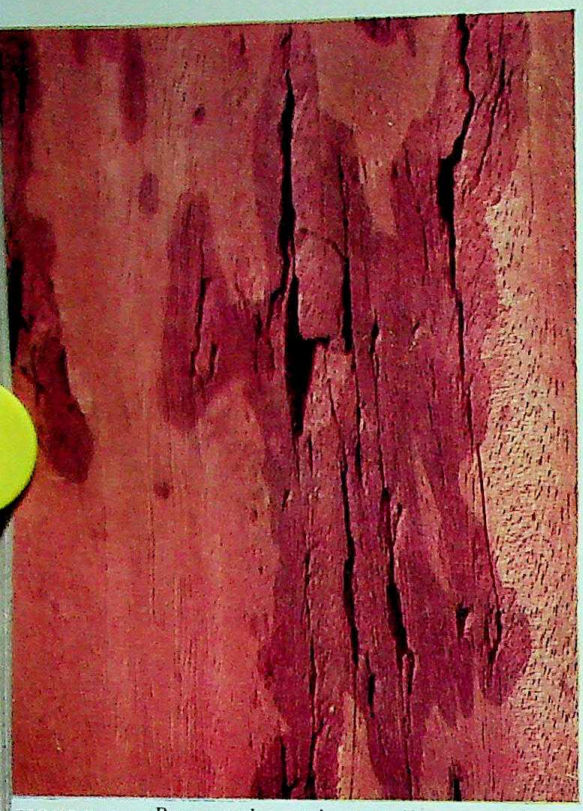


FIGURE 3 – *Brown pocket rot in opepe* (Sarcocephalus diderrichii).

FIGURE 4 – *White rot with pronounced zone lines in birch.*

FIGURE 5 – *White pocket rot caused by* Trametes pinicola *in imported Douglas fir.*

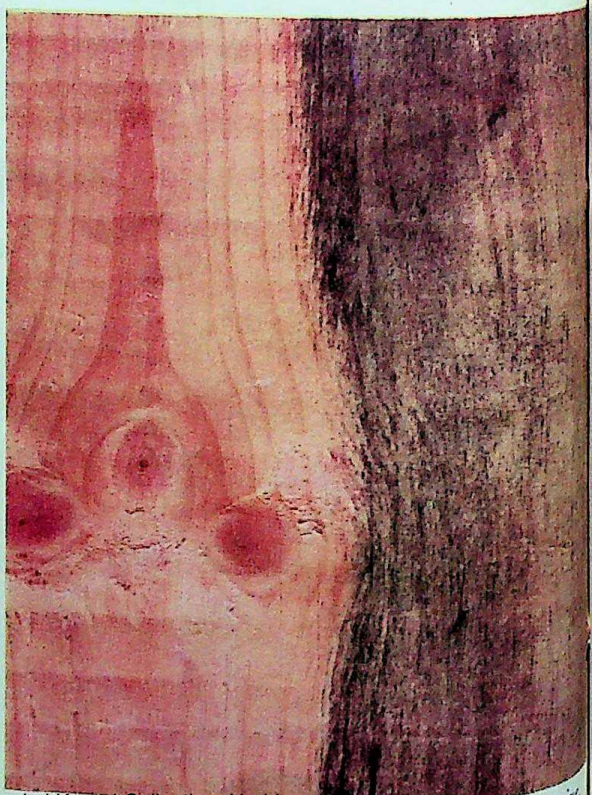


FIGURE 6 – *Sap stain ('blue' stain) in sapwood of pine caused by* Ceratostomella *sp.*

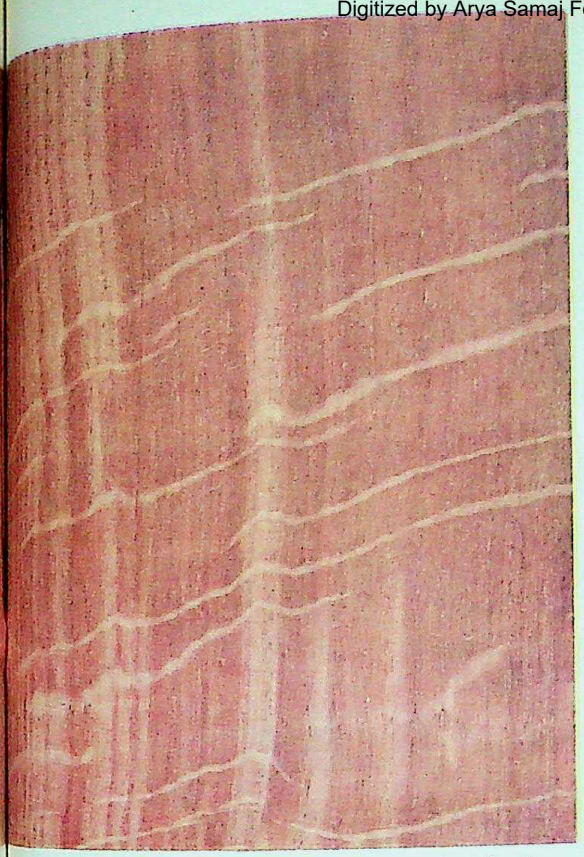


FIGURE 7 – *Brown oak. The warm brown coloration is caused by the beefsteak fungus,* Fistulina hepatica. *This wood of oak is often used for furniture of high quality.*

FIGURE 8 – *'Green oak': the colour is due to the fungus* Chlorosplenium aeruginosum. *This wood has been used for decorative inlaid work.*

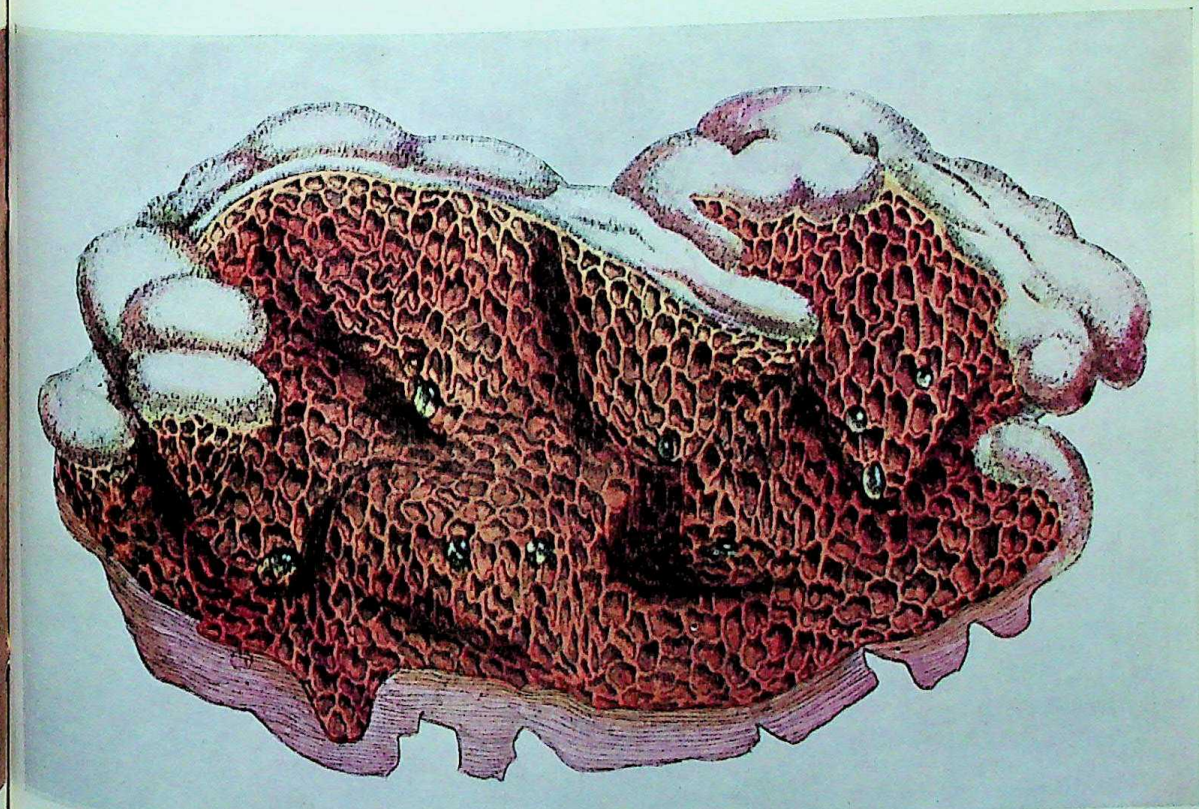


FIGURE 9 – *One of the earliest illustrations of the dry-rot fungus* Merulius lacrimans (*plate* 113 *of Vol.* 1 *of Sowerby's* Coloured Figures of English Fungi or Mushrooms, 1797). *Sowerby describes the fungus as 'much too common in England . . . as the fructification is seldom without drops of water resembling tears the Latin name* lachrymans

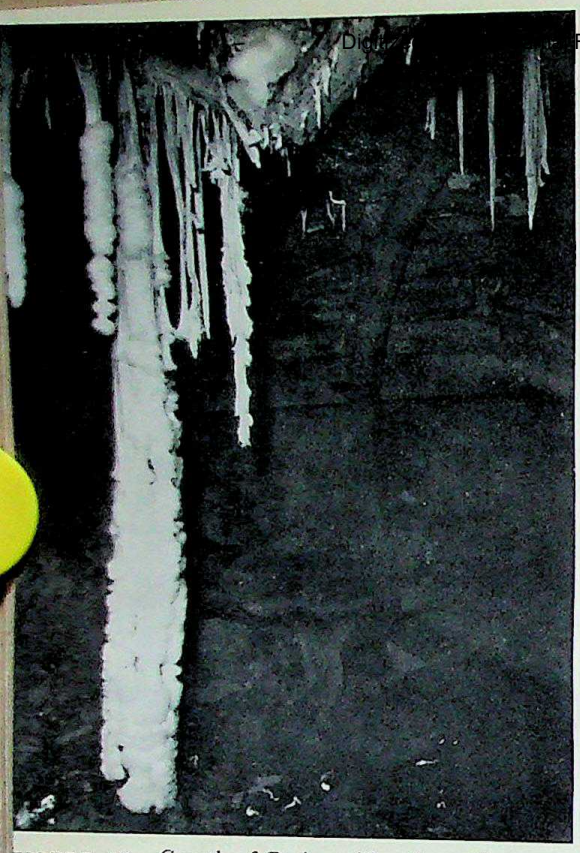


FIGURE 10 – *Growth of* Poria vaillantii *mycelium on decaying pit props in a coal mine.*

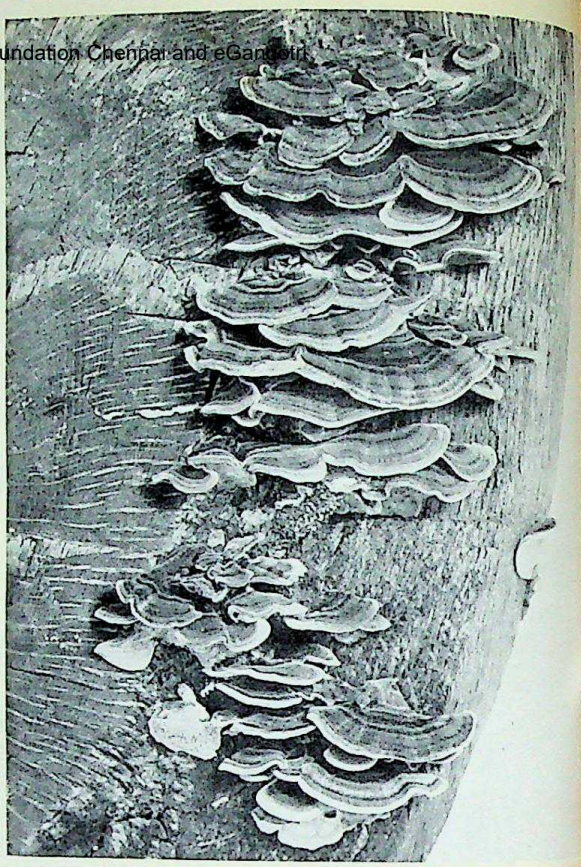


FIGURE 11 – *Sporophores of* Polystictus versicolor *on sapwood of oak log. Note absence of fungal growth on the heartwood.*

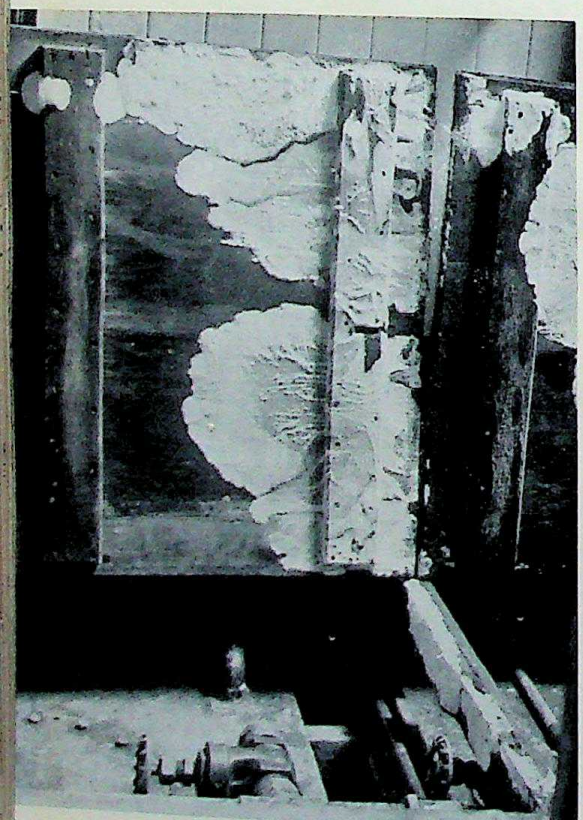


FIGURE 12 – *Fungal growth on wood floor above water tanks in motor launch.*

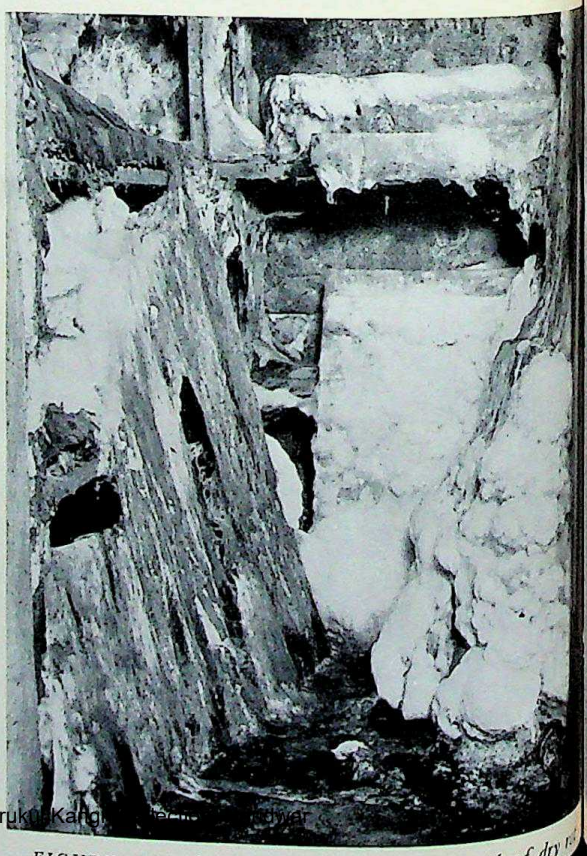


FIGURE 13 – *An exceptionally vigorous growth of dry rot fungus* (Merulius lacrimans)

could have been prevented had the conditions that lead to dry rot been more widely understood by the general public, and had simple precautions been taken to dry out buildings into which leakage of water had occurred. Architects and builders are now becoming increasingly aware of the need to prevent moisture reaching woodwork and setting up conditions favourable for dry rot, and plans for the new types of houses—both of prefabricated and of traditional types—are scrutinized from this point of view. The use of timber impregnated under pressure with wood preservatives is also steadily increasing. It is therefore most unlikely that the buildings now being erected will suffer from dry rot to the same extent as those built during the past century.

In many mines, decay of the pitwood has in the past been rapid and the cause of increased charges (see figure 10). The Transvaal Chamber of Mines, convinced that substantial saving can be effected by proper preservative treatment of timber used in the gold mines of the Rand, has established a special timber research laboratory. An interesting sidelight on the value of timber preservation in these mines was the discovery that the fungus responsible for a serious skin disease of the mine-workers—sporotrichosis—could be controlled by preservative treatment of the pit-props, which not only prevented the growth of wood-rotting fungi but also inhibited the development of the pathogenic mould that causes the skin disease.

During the war, large numbers of wooden vessels were built, and experience with certain types has shown the need for preservative treatment of any woodwork that cannot be adequately ventilated. Many private yachts were laid up for years and suffered much deterioration from decay that would not have occurred had the appropriate preservative treatment been applied to the vulnerable parts (see figure 12).

The story of the campaign for the proper packing and preservation of stores destined for the tropical theatres of war, the so-called 'tropicalization,' has been told elsewhere, but we are still finding evidence of the need to 'preserve' packing cases for stores that have to be kept for lengthy periods in the open, or in damp or ill-ventilated stores, such as underground mine workings or quarries.

PREVENTION OF DECAY IN LOGS

Less timber than formerly is now available from the Baltic countries and Russia, and the countries of western Europe are looking to the forests of Africa and South America to supply the deficiencies. In former times, the bulk of the timber from tropical countries consisted of such species as teak, mahogany, greenheart, and other durable or relatively durable species, which could be shipped without serious risk of deterioration between the time they were felled and the moment when they were sawn up in this country. Today there is also a demand for the softer, light-coloured woods from these countries—the so-called 'soft hardwoods'; but many of these species are attacked very quickly after felling by wood-boring insects, and by fungi that cause either disfiguring stains or decay. Practical methods for preventing this deterioration are being studied in West Africa, and some measure of successful control has already been obtained in experiments with logs sprayed with emulsions of pentachlorophenol and benzene hexachloride.

NEED FOR EDUCATION AND DEVELOPMENT WORK

In most countries, forestry has been the poor relation of agriculture, and forest utilization problems have seldom received the concentrated study that has been given to agricultural problems of a similar nature. Yet the adequate scientific and technical information now available could enormously raise the standard of timber utilization, and prevent by far the greater part of the needlessly rapid deterioration that all too often takes place. It is not implied that there is no need for further research on the pathology and preservation of timber—on the contrary, there is an urgent need for extended work in this field, especially under tropical conditions, where termites are responsible for at least as much damage as fungal decay—but with the knowledge and methods already available a very great deal more can and should be done to reduce needless waste of good timber through premature decay.

Flight at supersonic speeds

S. G. HOOKER

Flight at speeds greater than that of sound presents many problems to the aircraft designer and engineer. Dr Hooker explains that, for the designer, one of the most serious difficulties is that an aircraft built to fly at supersonic speeds at high altitudes becomes unmanageable at low altitudes and at the much lower speeds necessary for landing and taking off. For the engineer, the major problem is the provision of a compact power unit capable of generating the great power necessary to overcome the high drag experienced at these speeds.

Announcements in the United States press have told us that a number of American pilots have now flown, in level flight at high altitudes, a special rocket-propelled aircraft at speeds greater than the velocity of sound; more recently a British pilot, Mr. John Derry, has exceeded a Mach number[1] of unity in a dive, flying the De Havilland 'Swallow' jet-propelled aircraft.

The research work carried out by the Germans during the recent war in the field of supersonic flight, impressive in its quantity, quality, and breadth of vision, adds to the signs and portents of our time that a new era in flight is approaching —the supersonic era. Britain is not likely to lag behind in these developments.

Until 1940 the speed of aircraft had been limited to about 400 m.p.h., or 0·55 Mach number, and no appreciable advance on these figures seemed probable or possible with the conventional type of power plant consisting of an airscrew and reciprocating engine.

THE JET ENGINE

The advent of the jet engine, however, completely changed the picture. Here was a new power plant—light, compact, enormously powerful, and, moreover, possessing the very desirable property of propulsive efficiency increasing with forward speed. In a few years the world's speed record has risen from 55 per cent. of the speed of sound to more than 85 per cent., and high Mach number effects in the airflow about the wings and body have passed from the realm of mathematical curiosities to become dangerous realities.

What are these peculiar conditions that arise as we approach and exceed the velocity of sound? How do they affect our conception of the supersonic aeroplane of the future? Concerning these questions much remains to be learned from research, and more from the practical application of known results to the design of aircraft, but the broad lines upon which the progress in design must develop are already fairly firmly established.

Let us consider the peculiar circumstances arising when a body travels through the air at speeds greater than the velocity of sound. By definition, the velocity of sound is the speed at which small pressure disturbances caused by a body will be propagated in all directions, and it is these pressure disturbances which make the presence of the body felt in the surrounding atmosphere. Evidently, if the speed of the body is greater than that of sound, then the air ahead of the body will be completely 'unaware' of its approach. In the upper diagram of figure 1 let A_1, A_2, A_3, A_4 be successive positions of the body travelling in the direction indicated with speed U greater than sound. Then, while the body moves from A_1 to A_4, the disturbance caused by its nose will have travelled at the speed of sound to all points on the circle of radius A_1P_1; and similarly during the interval between A_2 and A_4 a circle of disturbance of radius A_2P_2 will be formed. Evidently the complete disturbance caused by the nose of the body will be confined between the lines A_4B_1 and A_4B_2, which thus constitute waves making angles of $\sin^{-1}(a/U)$ to the direction of motion. These limiting waves are the envelope of all disturbances originating from the nose of the body in its passage in the direction indicated, and they are propagated normal to themselves at the speed of sound. The air external to the angle formed by A_4B_1 and A_4B_2 is completely unaffected by the approach of the body.

Extending the above argument to a wing, as in the lower diagram of figure 1, every point on the wing surface will propagate a sound wave inclined at an angle $\sin^{-1}(a/U)$ to the direction of motion, and the picture of the disturbance caused by the

[1] By Mach number (M) we mean the ratio of the speed of the aircraft to the velocity of sound.

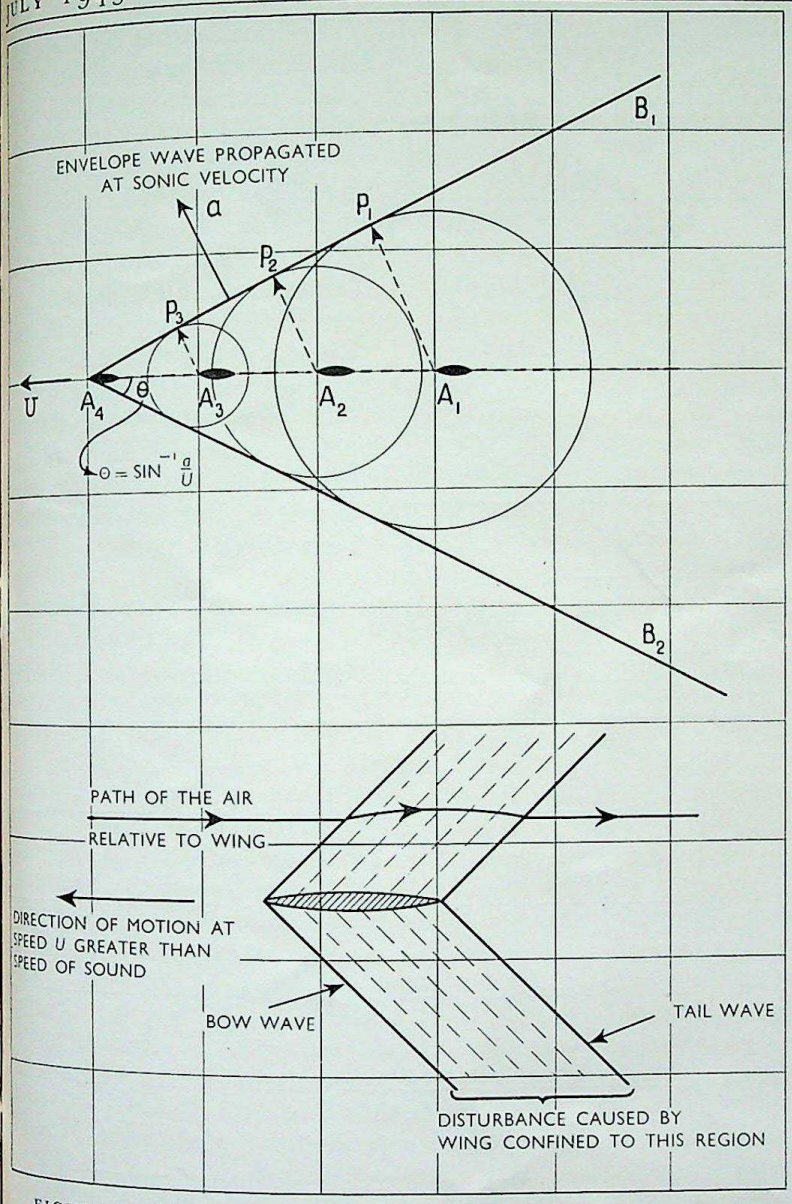


FIGURE 1 – *Wave formation set up by wing travelling faster than sound.*

wing will be as indicated. It is confined solely to the region between the bow and tail waves, and, in fact, the wing disturbance is attached to, and travels along with, the wing itself—in contradistinction to conditions below the speed of sound, where the disturbance precedes the wing and spreads to all regions of the surrounding atmosphere at the speed of sound. The fact that the wing is continuously generating this wave system as it travels on its course is responsible for the very large drag which is experienced.

DESIGN AT SUPERSONIC SPEEDS

The diagrams in figure 2 show the changes in design which may be expected as we reach and exceed the speed of sound. Firstly, in regard to the wing, or aerofoil, section. At speeds up to $M = 0{\cdot}7$ we have the conventional section designed to produce high lifts, having the upper surface more highly cambered than the lower. As we approach the speed of sound, the section should get thinner and tend to become symmetrical, having its maximum thickness at about half the chord. Finally, the supersonic section will be symmetrical, and will have sharp leading and trailing edges.

As a result of these changes, the drag coefficient will change as indicated. Up to about $M = 0{\cdot}8$ the coefficient will be unaffected by Mach number, and will stay at its low-speed value. Between $M = 0{\cdot}8$ and $M = 1{\cdot}0$ a rapid rise in drag coefficient will occur—reaching, perhaps, a figure five times as great as the low-speed value—and finally, at supersonic speeds, a decrease will occur, to about twice the low-speed value, at velocities greater than twice that of sound.

The plan form of the wings will also undergo radical changes. As we approach $M = 1{\cdot}0$, wings will be swept back at angles up to 45°, because this has been found to delay the onset of wave formation on the wing surfaces. The chord of the wing will be increased and the span of the wing decreased, because wings of low aspect ratio have been found to be less susceptible to wave formation.

Finally, at supersonic speeds, the leading edge will be swept back at a greater angle, up to 75°, and the plan form will tend to become triangular. Such a change will evidently result in great structural advantages—features very welcome in helping to overcome the large aerodynamic forces involved at such high speeds. It is more than probable that the ordinary tail will disappear altogether.

It may well be asked why these changes are so long in coming about. The answer is not far to seek. Aircraft have, of necessity, to take off and land

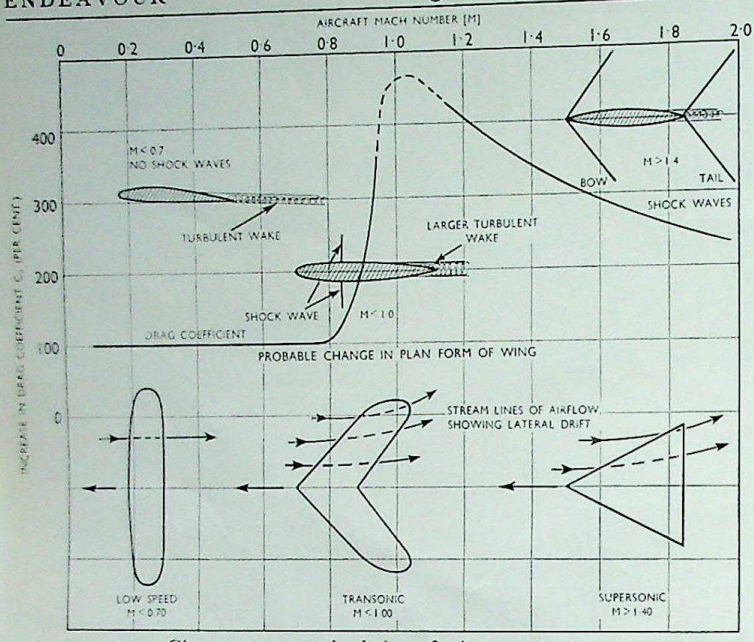


FIGURE 2 – *Changes necessary in design of wing as Mach number increases.*

at a moderate speed—say about 120 m.p.h., and while the changes indicated above are all advantageous at high speeds, they are almost as big a disadvantage under landing and take-off conditions. One of the most important difficulties is that the tips of the swept-back and triangular wings tend to stall first, thus causing a serious loss of control. The reason for this tip-stalling is that the airflow drifts outwards towards the wing tip owing to the inclined leading edge and, in fact, tends to slide off the wing tips laterally without producing any lift (see figure 2).

The take-off difficulty could, of course, be overcome by launching the supersonic aircraft from a 'mother' aircraft, as has been done in Britain in experiments using pilotless models. Alternatively, a rocket-propelled carrier on rails could be employed, similar to the system used by the Germans for launching the V1. Landing would be much more difficult, and parachutes might have to be used for the final descent.

No mention has been made of the type of fuselage for a supersonic aircraft, and this abominable but necessary excrescence must be reduced to an absolute minimum, so as to reduce resistance and not to disturb the aerodynamic flow. To keep the frontal area as small as possible, it is probable that the pilot and crew will have to lie prone. In this position the human body is best able to withstand the physical effects of the very high accelerations which are bound to occur during any manœuvring at these high speeds.

THE SO-CALLED SONIC BARRIER

The expression 'sonic barrier'

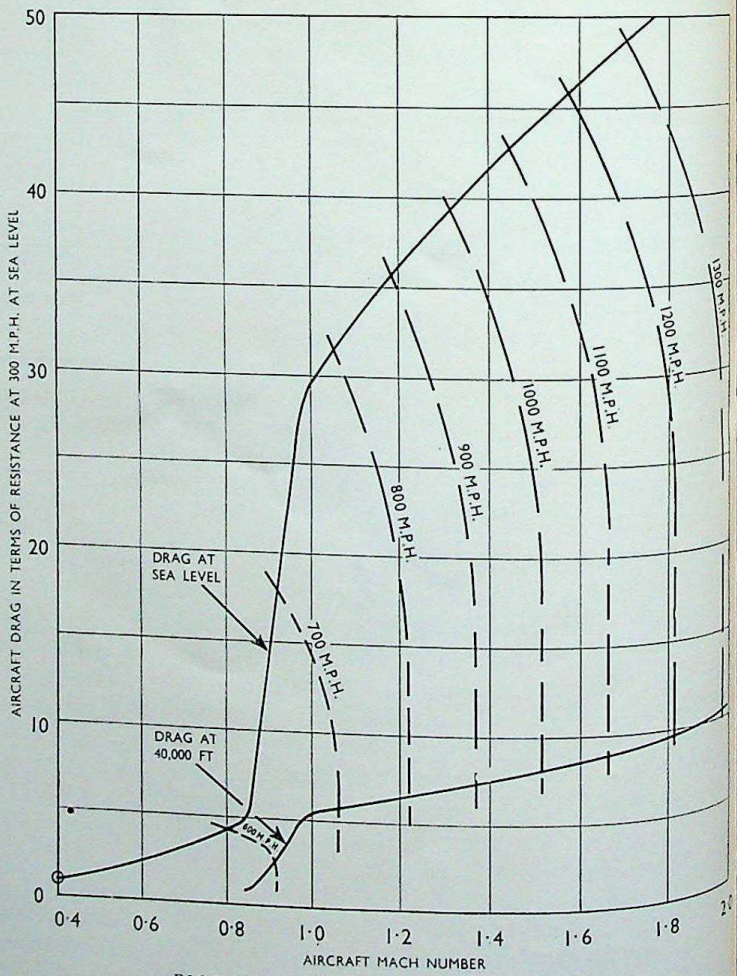


FIGURE 3 – *Air resistance at supersonic speeds.*

has become quite common, but we should not delude ourselves into thinking that there is a magic wall of air resistance occurring at the speed of sound, through which the aircraft must be forced, and that, once through, all will be plain sailing with no head wind. In fact, the air resistance increases continuously with speed, and the drag coefficient C_D shown in figure 2 must be multiplied by the air density ρ and the square of the aircraft speed V before the actual drag is obtained; thus:

$$D = \rho V^2 C_D$$

But the density of the air is proportional to its pressure p divided by its absolute temperature, and we can write:

$$D = p\frac{V^2}{T}C_D$$

Continuing, we know that the velocity of sound is dependent only upon the square root of the absolute air temperature, so that finally the drag is given by

$$D = KpM^2C_D,$$

where M is the Mach number of the aircraft.

Using the above equation and the form of C_D given in figure 2, we can construct the aircraft drag in terms of the resistance experienced at 300 m.p.h. (0·4 Mach number) at sea level. Note that the above equation shows that, at any given Mach number, the aircraft drag is proportional to the altitude pressure only. Figure 3 shows the calculated drag at sea level and at 40,000 ft. plotted against the aircraft Mach number.

Thus, at 1·8M at sea level the aircraft drag is 50 times as great as at 0·4M. To illustrate the point, a machine of the size of the Spitfire has a drag of about 1,000 lb at 300 m.p.h. at sea level. Doing our best with the aerodynamic form of the wing, an aircraft of this size would have a drag of 50,000 lb at 1·8M at sea level, and as this Mach number corresponds to 1,365 m.p.h. the thrust horse-power required would be no less than 182,000—rather more than it takes to propel the *Queen Elizabeth*! (Incidentally, the German V2 rocket developed a thrust of 60,000 lb within a diameter of 5½ ft.)

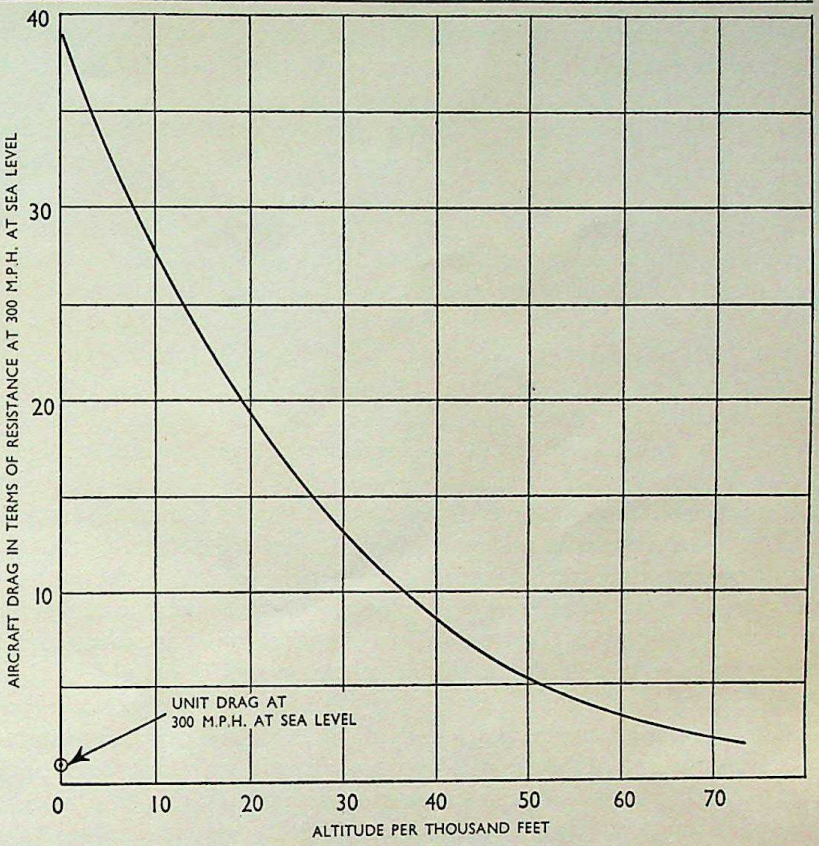


FIGURE 4 – *Drag on aircraft flying at* 1,000 *m.p.h.*

Assuming propulsion by a jet engine, the fuel consumption would be at the rate of 90,000 lb per hour. Evidently the horse-powers involved rule out completely the conventional airscrew and reciprocating engine.

Propulsion by rocket is even more expensive in fuel, the consumption being no less than 900,000 lb per hour for a thrust of 50,000 lb—ten times that of the jet engine.

Obviously supersonic flight at sea level will be possible for only a matter of seconds, owing to the high consumption of fuel, whatever type of engine is employed; and it is doubtful if enough fuel can be housed for the four consecutive runs (two in each direction) which have to be made over the measured kilometre at sea level in order to qualify for the world's speed record.

FLIGHT AT HIGH ALTITUDES

The picture changes if we go to higher altitudes into the region of thinner air. Figure 3 shows that at 40,000 ft, where the air pressure is only 5·54 cm of mercury, the drag at 1·8M has fallen to 9·5 times the drag at 300 m.p.h. at sea level; that is, to the more manageable figure of 9,500 lb. This would require a consumption of rocket fuel of only

50 lb per sec, and, in fact, the fuel housed in the V2 (18,000 lb) would be sufficient for a six-minute flight. This same quantity of fuel would, however, last a jet engine for more than an hour—a fact which is encouraging from the practical point of view.

To fix ideas more definitely, let us forget Mach numbers and consider an aeroplane travelling at 1,000 m.p.h. Figure 4 shows its drag at all altitudes, where again the unit of drag is that at 300 m.p.h. at sea level. At 70,000 and 60,000 ft we are getting down to drags of two and three times our unit (i.e. 2,000 and 3,000 lb for the case previously considered), and evidently at these altitudes supersonic aircraft with practical endurances and ranges are a distinct possibility.

It will, of course, be necessary to pressurize the pilot's cabin, and since the atmospheric pressure at 70,000 ft is only 33 mm an air compressor having a compression ratio of 16 : 1 will be required to bring the pressure in the cabin up to that corresponding to 10,000 ft.

Strangely enough, even at these high altitudes one of our major problems will be to keep the pilot cool. Owing to the forward speed, any air picked up and dragged along by the aircraft will be heated by 100° C. This is not due to friction, but is merely the energy which has to be given to the air in order to accelerate it from rest up to 1,000 m.p.h. The fuselage and wing surfaces might be expected to be heated by 85° C, and since at 70,000 ft the atmospheric temperature is −57° C, the temperature inside the cockpit would be at least 30° C or 86° F. Added to this, we have the heat due to the compression of the air by the cabin supercharger, and even with the maximum amount of cooling that we could apply to this air, the pilot would be uncomfortably hot and dry.

ENGINES FOR SUPERSONIC AIRCRAFT

What of the engine for supersonic aircraft? There appear to be three possible types: a rocket motor, a jet engine employing reheat in the jet pipe, and an aerothermodynamic duct or, more shortly, an athodyd.

As we have seen, the great disadvantage of the rocket is its huge consumption of fuel, which is primarily due to the fact that it has to carry its own oxygen along with it in the form of one of the fuels. In all other respects it has every advantage. It is light, mechanically—but not structurally—simple, and develops the same thrust at 70,000 ft as it does at sea level (again due to the fact that it carries its own oxygen).

The thrust of a jet engine, on the other hand, falls off almost proportionally to altitude air density, and is further limited by the maximum temperature which can be used in the combustion chambers, because of the decrease in physical strength of the turbine blades at high temperatures. Consequently, only about one quarter of the available oxygen can be used before reaching the turbine, but there is no reason why the remainder cannot be utilized in the jet pipe after leaving the turbine, thus increasing the thrust available. By this means 70–80 per cent. extra thrust can be obtained without endangering the life of the turbine blades.

Finally, there is the athodyd, which is the simplest of all engines. The fundamental cycle for any heat engine is first to compress the working fluid, then heat it, and finally to expand it, and this is in effect what the rocket or the jet engine does. Now, the forward speed of an aircraft is capable of compressing the air it picks up. If we mount a duct on a high-speed machine and give it a forward-facing intake, correctly shaped to diffuse the air velocity entering it into pressure, then we can burn fuel in the duct, and, having discharged it rearwards, we shall obtain a thrust which can be made capable of propelling the aircraft. For example, at 1,000 m.p.h. a compression ratio of 3·5 : 1 is theoretically obtainable in this way. In fact, the aeroplane acts as its own compressor, and all we have to do is to heat the compressed air with fuel and expand it through a rearward jet. Evidently this engine is inefficient at low speeds, where the air compression is small, and will give no thrust under static conditions. It is useless for taking the aeroplane off the ground, and does not come into its own until the machine is actually travelling at supersonic speeds. While it seems unsuitable as the main power plant, it may yet prove valuable as a booster unit once supersonic conditions have been obtained by other means.

The garden at Tresco

J. W. HUNKIN

The great garden at Tresco, in the Scilly Islands, deserves to be much better known. It is now over a century old, and although it was severely damaged by tempest in 1929 the recovery was very swift. Sir Arthur Hill, late Director of Kew Gardens, described the garden at Tresco as an imperial asset of great importance. The Bishop of Truro, in whose diocese the Scilly Islands lie, here gives an account of it, with coloured plates specially taken.

The Isles of Scilly consist of more than three hundred rocks and islets, situated about thirty miles west of Land's End. Five only are inhabited; of these St Mary's is the largest, and Tresco, about two miles to the north across a broad roadstead, is the second. The scenery is on a small scale, but there is a wonderful freshness in the air, and the colours of the white sand, the blue and sapphire sea, the golden seaweed, the sea pinks, and the gorse and heather, have the brightness of a jewel.

The modern history of the Isles of Scilly begins in the year 1834, when Mr Augustus Smith of Berkhamsted succeeded the Duke of Leeds as lessee of the islands from the Duchy of Cornwall. Augustus Smith fell in love with Scilly, and ruled there as lord proprietor—'Emperor of Scilly,' as his friend, Lady Sophia Tower, used to call him—until his death in 1872. It was a firm and benevolent rule, and the islanders, who had been in a very poor way in the early years of the nineteenth century, came to enjoy considerable prosperity.

Augustus Smith decided to live on Tresco. When he arrived, there was nothing growing on the island above the height of a gorse bush, save in the little parsonage garden, where there were a few small stunted trees. He chose a site for his house near the ruins of the ancient abbey, a small outpost of the Benedictine Abbey of Tavistock in Devonshire (figure 6), and began planting for shelter. He also built a sheltering wall and stocked his garden with interesting plants, many of them too tender to be grown in the open on the mainland. Some of these plants were sent to him from Kew, and others came from correspondents in Australia, New Zealand, and South Africa, or were grown from seeds brought home by his friends among the sea-captains. He gradually increased his shelter belts, using *Quercus ilex*, *Cupressus macrocarpa*, and *Pinus radiata*, and he took more of the hillside into his garden until it included some twelve acres on the southern slope of the central hill of the island.

The garden has three main walks: the 'Top Terrace' of some 300 yards, east to west, near the top of the garden; the 'Long Walk' parallel to it on the level ground at the bottom; and the 'Middle Terrace,' a third parallel between the other two, and rather shorter. There are various paths and steps connecting the three. The main way down is by the 'Neptune steps,' leading straight from an old statue of Neptune (figure 5) on the Top Terrace to the Long Walk below, a distance of about seventy-five yards, and on, a further seventy yards, to the old brazier of the lighthouse on another of the islands (St Agnes), now set up by the south wall of the Tresco garden. Near this south wall, a little farther west, is a veranda known as 'Valhalla,' because it contains some seventy old figureheads or other relics of ships wrecked on the islands (figure 3).

These wrecks are a tragic reminder that the great enemy at Scilly is the wind. The storms are sometimes very violent. In the winter of 1929–30, for example, there were no fewer than fourteen occasions when the wind rose to over eighty miles an hour. The temperature, however, is very equable and mild, seldom outside the limits of 40–60° F; and the hours of sunshine average nearly five hours daily. There are ten inches less rain in the year than at Penzance, on the mainland some forty miles away, the average at Tresco being 32·4. As for the soil, it is a light mixture of sand and peat which tends to become very dry in summer.

From the first, the Tresco garden was unlike any other in the British Isles. Augustus Smith made good use of the rocks and great stones of the island and made his garden brilliant with masses of mesembryanthemum, of which he had scores of varieties—his 'mesmerisms,' as he used to call them—with their thick succulent leaves and starry flowers, large and small, of glistening white, bright yellow, red, and purple. Two quotations from letters written to Lady Tower in 1858 give

vignettes of the garden, one in winter and the other in summer:

> *3rd January*, 1858. This gentle winter has not been unfelt in my garden, which is a blaze of blossoms wondrous to behold; the *Veronica Andersonii*, Correas, Fuchsias, Genistas, and above all *Acacia lophantha* are covered with flowers; one of the last particularly, not less than twelve feet high and as many broad, along the Long Walk, is a perfect picture; the Sedums also, with their large yellow pyramids of bloom, each nearly as big as my lamp papers, are very ornamental . . . and a certain set of *mesmerisms* are also in flower.

> *1st June*, 1858. My garden is a blaze of blossom, especially as to Geraniums; more than usual survived last winter, and whole beds of *Unique*, especially, and other sorts are one mass of flower; . . . The *Dracaena indivisa* is fast advancing to perfection; the flower is not very conspicuous, but a mass of white feathery stems crowning the summit of the plant; the blossom is white; . . .

In 1872 Augustus Smith was succeeded by his nephew Thomas Algernon Dorrien Smith, a lieutenant in the Tenth Hussars. In 1875 he married Edith, daughter of his uncle's great friend Lady Sophia Tower. They had seven children, and at Tresco they resided for eight months in each year.

It was Thomas Algernon who started in the islands the cultivation of the narcissus for the market, an industry which has proved to be the most remunerative of all the islands' industries. The 'Scilly White' and the 'Soleil d'Or' he found growing about the Abbey ruins. Possibly they had been introduced by the monks. As an experiment he persuaded Mr Trevellick, who held a farm on St Mary's, to send up some flowers to Covent Garden. He put them in a hatbox and realized a pound for them. The first flower show to be held in the Isles of Scilly took place on Tuesday, 30th March, 1886, when Thomas Algernon showed upwards of 160 varieties of narcissus, arranged on a groundwork of green moss.

Meanwhile he had been developing the abbey garden. He discovered that *Pinus radiata* (*insignis*) stood the wind better than *Cupressus macrocarpa*, and he was able to establish a belt of shelter on the south-west side of Tresco hill. The plants in the garden continued to flourish and grew larger and larger. Some which Augustus had never seen in flower came into blossom in the 'seventies and 'eighties. *Furcraea longaeva* was one of the most striking of them. From a yucca-like base it shoots up a very tall stem with slender branches bearing its cream cup-like flowers. The *C. macrocarpa* along the abbey drive formed itself into a huge hedge of beautiful and unusual green fifty feet high, which it took a fortnight every year to clip.

Thomas Algernon died in 1918, and the present owner, his eldest son, Major Arthur Dorrien Smith, D.S.O., succeeded him. The Major had already made his mark in the horticultural world, particularly by introducing from the Chatham Islands the finest of all the olearias, *O. semidentata*, with its great, lovely, purple, daisy-like flowers. He had travelled extensively in South Africa, Australia, and New Zealand, and had sent and brought to Tresco a large number of seeds and plants of various kinds.

Sir Arthur Hill, the late Director of Kew, wrote a short account of the garden in the *Kew Bulletin* (1920, No. 5), and after mentioning various species of acacia, melaleuca, hakea, *Leucodendron argenteum*, *Araucaria excelsa*, and the mesembryanthemums and pelargoniums of many colours and sizes flourishing as in their native homes, Sir Arthur concluded by describing the garden as 'an imperial asset of great importance to the botanists of this country whose work lies with the botanical resources of the British Empire.'

Some nine years later, in December 1929, the garden was devastated by a terrific tempest. On a Wednesday the gale was 93 miles an hour from the south-east, on the Friday above 110 miles an hour from the south-west, and on the Sunday 91 miles an hour from the north-west. The velocity of the wind did not fall below 70 miles an hour for more than eight hours during five days. Major and Mrs Dorrien Smith were away on the mainland at the time, and when they finally reached home in a torrent of rain they could hardly find their way. Paths were blocked and obliterated; trees, uprooted, had come crashing down on bushes and beds, and the ground was thickly strewn with branches and debris. Even the ilex had been stripped. Happily the recovery was far more rapid than one could have dared to hope.

In 1935 a beginning was made in compiling an official list of plants cultivated in the garden. Among the most interesting items are the following:

Acacia: 39 species.
Agave: 69 species, mostly from Mexico.
Aloe: 60 species.
Cistus: At least 15 species.

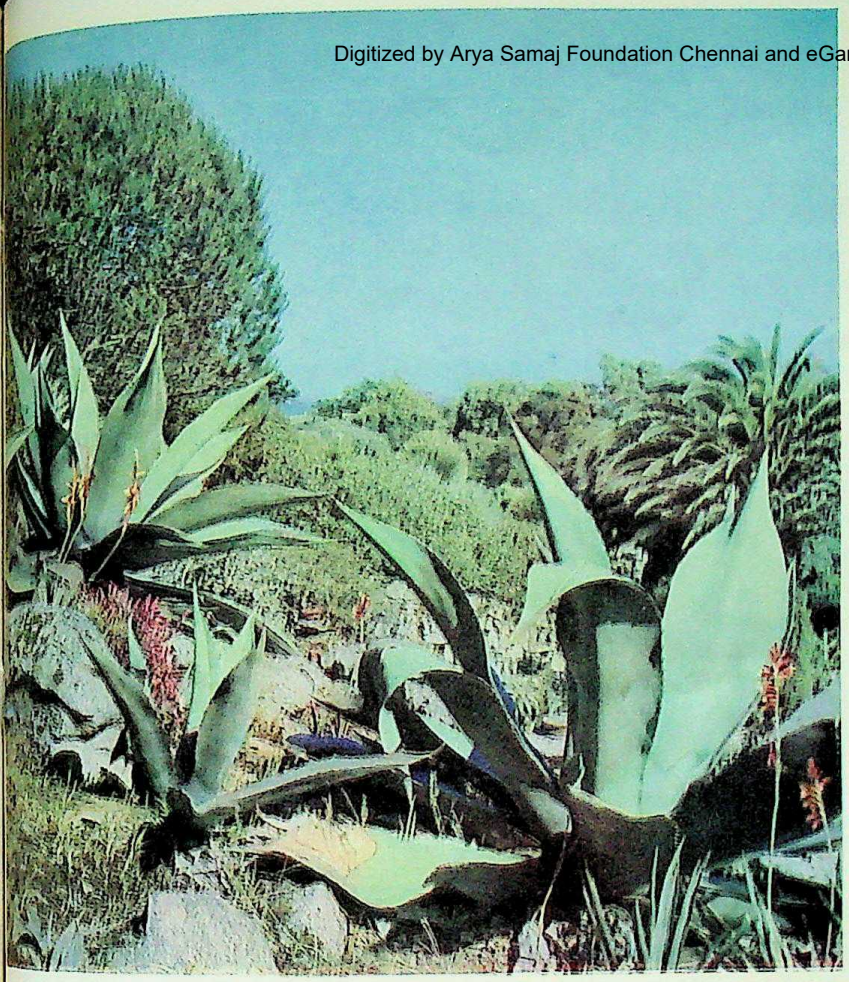


FIGURE 1 – Agave applanata, *wi* Phoenix canariensis *in the bac ground on the left.*

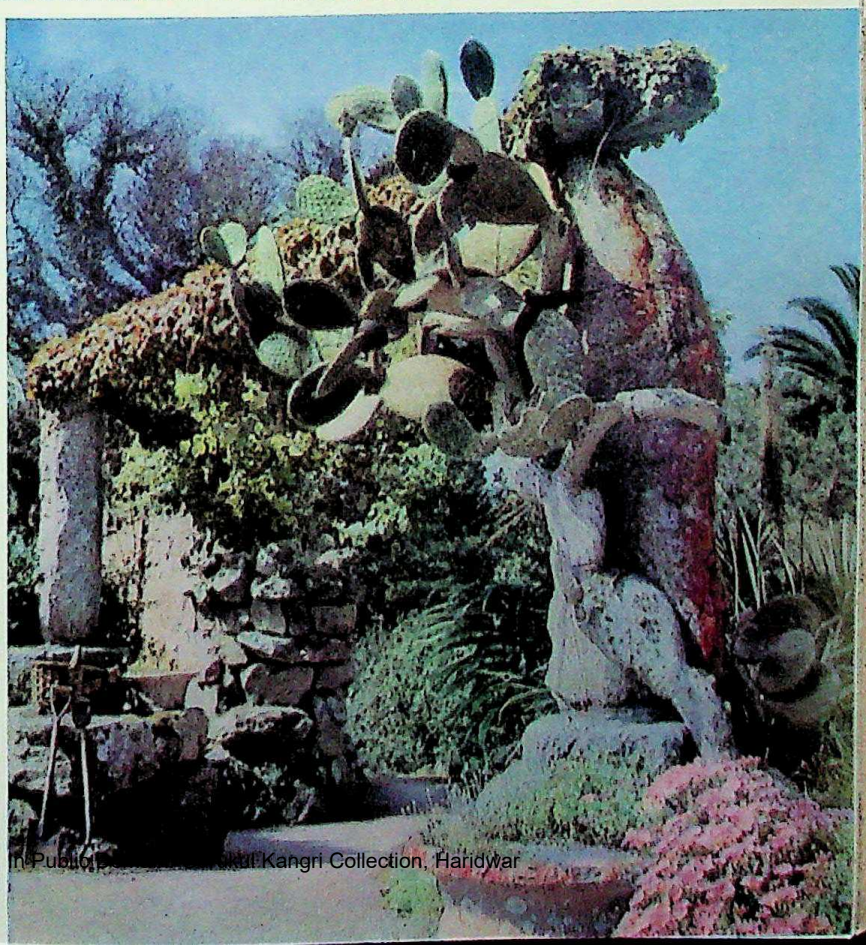


FIGURE 2 – *Prickly pear* (Opuntia occidentalis) *on the Middle Terrace.*

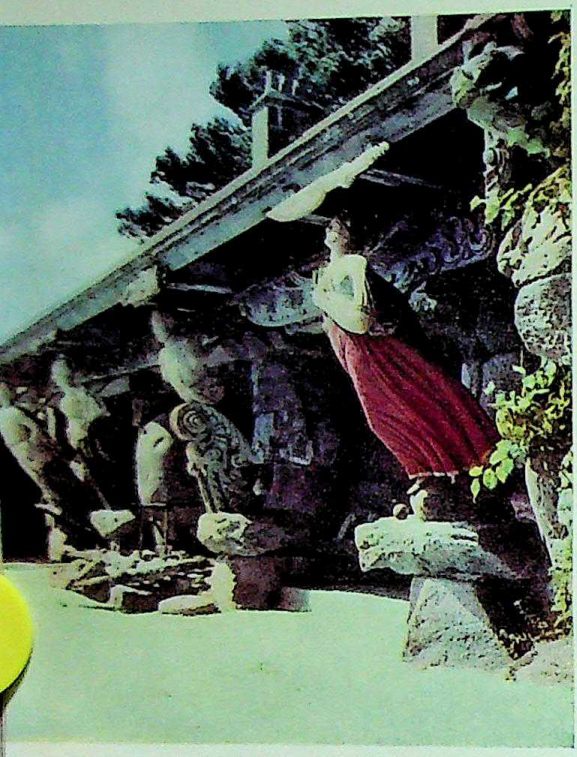


FIGURE 3 – *Ships' figureheads in 'Valhalla.'*

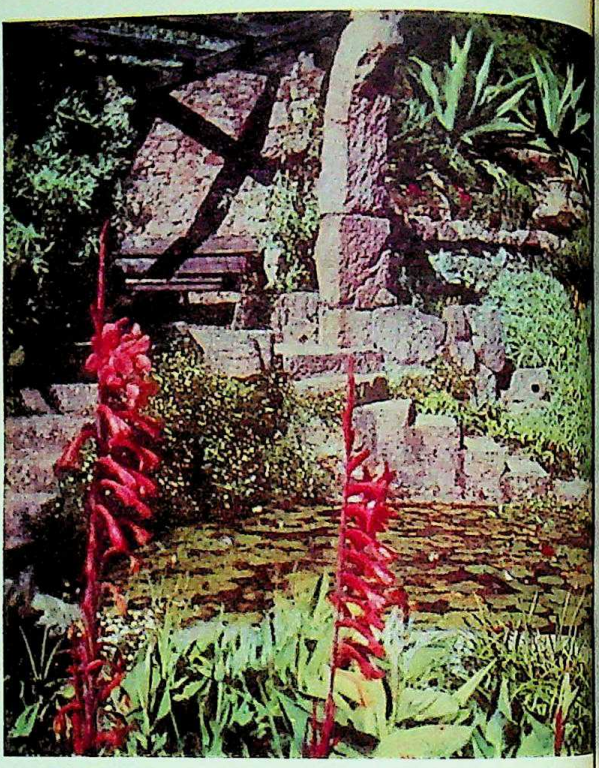


FIGURE 4 – *Lily pond on the Middle Terrace.* Watsonia Beatricis *in the foreground.*

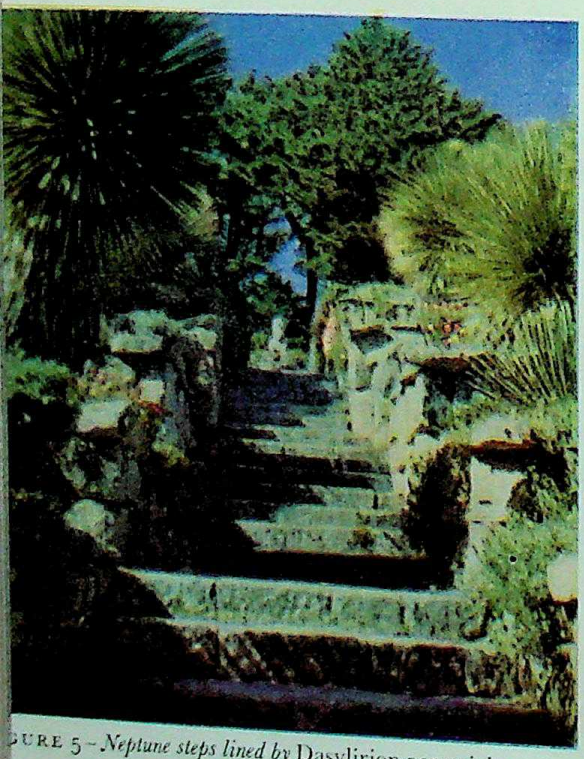


FIGURE 5 – *Neptune steps lined by* Dasylirion acrotrichum.

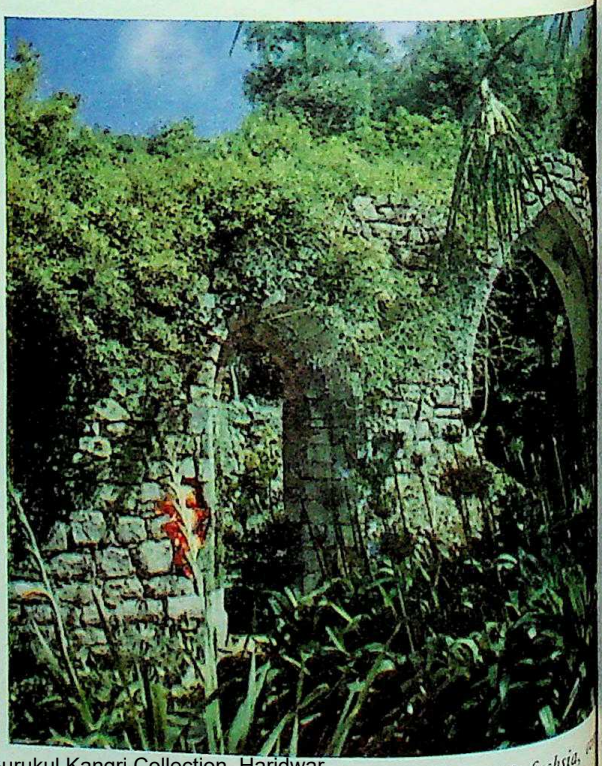


FIGURE 6 – *Polyanthus rose, veronica, and fuchsia, [illegible] arches of the ancient abbey.*

Coprosma: 12 species, including *Baueri* with its handsome thick, shining leaves.
Cytisus: 21 species.
Echium: 7 species.
Eucalyptus: 29 species.
Fuchsia: 28 species, including *cordifolia*, *fulgens*, *splendens*, *triphylla*, and garden varieties.
Hedychium: 8 species, including *coronarium* and *Gardnerianum*.
Leptospermum: 11 species, including the Australian tea-tree (*L. laevigatum*).
Mesembryanthemum: 153 species.
Metrosideros: *diffusa*, *lucida*, *robusta*, *tomentosa*.
Olearia: 33 species.
Opuntia (prickly pear): 14 species.
Pelargonium: 159 species and distinct varieties, in charming groups all over the garden. Many have scented leaves.
Pittosporum: At least 18 species.
Rhododendron: 135 species including *Dalhousiae*, *Veitchianum*, *etc.*
Senecio: 34 species, including *grandifolius*, *Kirkii*, etc.
Veronica: 62 species.

There are also many cacti and succulents, bottle brushes, and Proteaceae.

For many years one of the great sights in the garden was the scarlet of the many fine trees of *Metrosideros tomentosa* blazing far out to sea in July. All these were badly scorched by the unusual frost at the beginning of 1947. When the frost came, in January, the garden was gay with the red spikes of many aloes. They were demolished at once. The great tender-looking clumps of *Sparmannia africana* were in full blossom, and their white flowers with golden stamens withered away too. Most of the Tresco plants, however, even when badly injured, were not absolutely killed. Perhaps the two most notable fatalities were the karaka and the puka, both from New Zealand, on the Long Walk. The immense lustrous green leaves of the latter will be greatly missed. On the whole, however, the recovery has been remarkable, and when I was in the garden early in June 1948 I was delighted to find it still its lovely and gracious self. Half a dozen puyas were holding aloft their enormous yellow-green spikes, the dracaenas had their heads full of flower with the effect of deliciously scented lace, and the clumps of mesembryanthemums dazzled the eye.

The coloured photographs give a good idea of the sub-tropical appearance of the garden. Figure 1 shows some of the great American agaves, and with them must be imagined the African aloes, the red spikes of which make the garden gay in January. In the background on the right of the picture is one of the magnificent Canary Island Palms, several of which were planted in 1908. Their giant fronds rise from a single main trunk which bristles with the remains of former fronds. In the crevices thus formed grow various self-sown little plants: *Veronica*, *Pittosporum*, and, strangest of all, *Metrosideros tomentosa*.

The dasylirions in figure 5 are stiff desert plants from Mexico, with narrow spiny-margined leaves. They withstood the frost of 1946–7 without damage, and in the succeeding summer a dasylirion in another part of the garden shot up its high spike of greenish flowers in an astonishing manner.

The *Watsonia Beatricis* in figure 4, with its rich apricot-red flowers, is one of a number of Watsonias in the garden. They are summer-blooming bulbs from South Africa, like aristocratic gladioli.

Fuchsias and veronicas of many bright colours (figure 6) are a great feature in the garden. A species of the latter with attractive blue and white flowers is called after the Major: *V. Dorrien-Smithii*. The shrubby New Zealand speedwells which are commonly included under the name *Veronica* are now to be called *Hebe*. The figure shows one of them: *Hebe Dorrien-Smithii*.

The generous hospitality of this unique botanic garden is still maintained by the public-spirited family who have developed and cared for it for over a hundred years. The notice composed by Mr Augustus Smith may still be read on a slab of slate just inside the gate at the end of the Abbey road:

> All islanders are welcome to walk in these gardens, but are requested to keep to the main walks, not to go up to the house nearer than the under terrace in front, and to abstain from picking flowers or fruit, scribbling nonsense, and committing suchlike small nuisances. Enter then, if it so please you, and welcome.

Science in the detection of crime

H. S. HOLDEN

Science is an important and often indispensable agent in the detection of crime. The methods and processes employed have nothing novel in themselves, and are already familiar to scientists in general. The interest of the subject lies in the particular applications to which science is directed, and in this article, by the detailed consideration of specific cases, Dr Holden (of the Metropolitan Police Laboratory at New Scotland Yard) shows how scientific investigation assisted in the solution of certain apparently insoluble criminal problems.

The employment in Britain of the specialized knowledge of the scientist in the detection of crime has, in the past, been relatively restricted except in certain well-defined types of case, although many of the methods characteristic of science—for example, accurate observation, the correlation of all available data, and reasonable inferences from such data—are commonplaces of all criminal investigation.

The type of scientific specialist first employed by investigating officers was, as might be anticipated, the expert in forensic medicine. His collaboration was essential in all cases coming under the general head of crimes against the person, such as crimes of violence and the whole range of sexual offences. Among the crimes in which the help of the medical expert was sought it was inevitable that there should be some in which poison was suspected to be the cause of death, and the analysis of the organs and body fluids necessary in such cases involved the co-operation of the toxicologist. The scientific study of poisons was first established on a sound basis just over a century ago, with the publication of Taylor's *Handbook of Poisons* in 1848; since that date progressive refinements in technique have been developed which enable the toxicologist to isolate, identify, and determine the total amount in the organs examined, even when the quantities are relatively minute. Toxicology is, of course, only one highly specialized branch of one particular science, and within the last twenty-five years police forces have come to realize that the services of scientific experts covering a much wider field may be utilized with advantage, not only in the types of crime which make headline news, but also in the relatively prosaic day-to-day offences such as housebreaking, larceny, forgery, road-traffic accidents, and the like.

The beginnings of this wider use of the scientist in British criminal investigation are to be traced to the institution of the small laboratories established by individual police forces in various parts of the country, notably at Derby, Bristol, Cardiff, and Nottingham. These laboratories did admirable pioneer work, employing the scientific staffs of local universities, university colleges, and technical institutes as consultants, but the areas they served were necessarily limited. It became increasingly clear that there was a real need for an extension of laboratory work of this kind to serve the country as a whole. Careful consideration of the steps necessary to provide such a national laboratory service was given by the Departmental Committee on Detective Work and Procedure appointed by the Home Secretary in 1935, under the chairmanship of Mr A. L. (now Sir Arthur) Dixon, C.B., C.B.E.

Largely as a result of the deliberations of this body a number of regional forensic science laboratories under Home Office control have been established, covering the whole of England and Wales. These laboratories are situated at Preston (North Western Region, including North Wales), Wakefield (North Eastern Region), Nottingham (East Midland Region), Birmingham (West Midland Region), Cardiff (South Wales Region, including Monmouthshire), and Bristol (South Western Region) respectively. The laboratory serving the Metropolitan Police District and south-east England is at New Scotland Yard, London.

The staffing and equipment of each laboratory are such as to enable it to deal with most of the material likely to be submitted by investigating officers. Provision is, however, made for obtaining the services of outside experts, notably those of skilled forensic pathologists, where the crime under investigation requires their collaboration. Close and friendly contact with the police forces of the region is maintained through the liaison officer, who is normally a detective officer of senior rank with a good scientific background and who can often advise his police colleagues on the collection

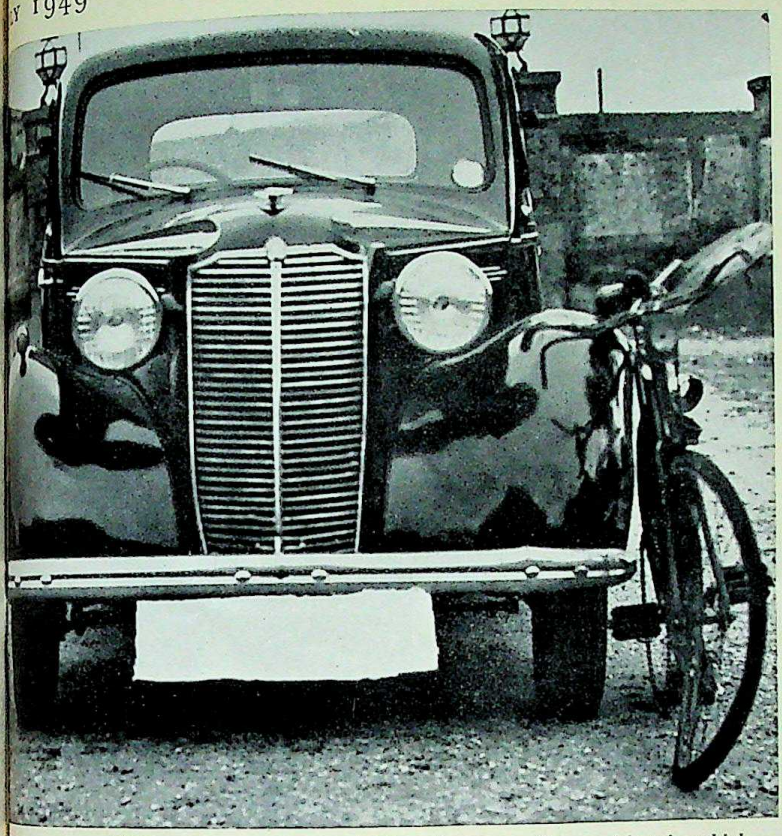


FIGURE 1 – *This car was suspected of being the cause of an accident in which a cyclist lost his life. The front nearside mudguard was damaged and a good deal of the paint had been lost.*

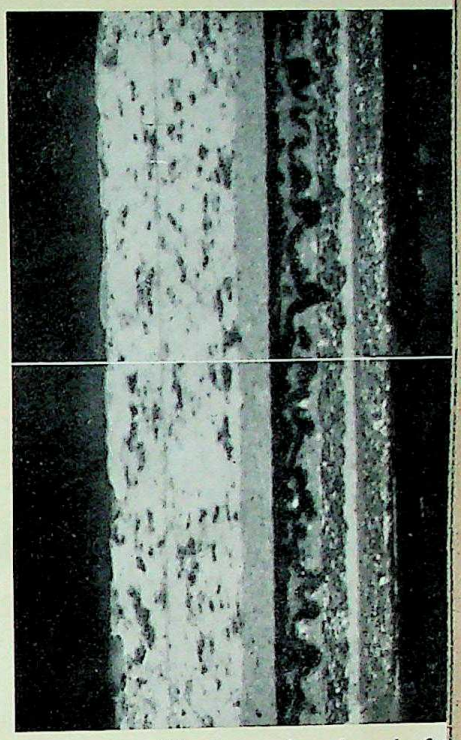


FIGURE 2 – *The damaged mudguard of t illustrated in figure 1 had been repainted times, as revealed by a section of the layer of on it, seen highly magnified at* (a). *A sectio flake of black-surfaced cellulose paint collected the scene of the accident is shown at* (b). *T quence of colours and the thickness of the proved identical with those of* (a).

and packing of material for laboratory examination. Detective officers are also given systematic instruction on the types of case in which help may be expected from the regional laboratories as part of the Government-sponsored detective training courses held in London and at a number of provincial centres. These lectures, given by the scientific and liaison officers, are followed by practical demonstrations and discussion, thus providing a valuable means of establishing a sound relationship between the scientist and the investigating officer. Informal talks on recent cases, and visits to the laboratories for the purpose of seeing work in progress, constitute additional methods of giving the officer an insight into the part the careful scientific examination of material may play in crime detection.

Experience has shown that the examination of the bulk of the material submitted to the laboratory falls within the realm of either chemistry or the biological sciences, although from time to time the help of the physicist and geologist is necessary.

The chemist, owing to the wide range of his subject and its many points of contact with other subjects, must necessarily play an important part. Toxicological examinations involve not only a knowledge of complicated and delicate analytical methods, and the recognition of both organic and inorganic poisons, but the ability to identify all kinds of drugs, including the many medicinally important organic synthetics. Other examinations will demand a similarly extensive knowledge of dyestuffs, paint pigments, and colours used in inks, cosmetics, and the like. In cases of arson and other types of incendiarism the ability to recognize all types of inflammable material, explosives, and explosives residues is essential. It is equally clear that much of this work will involve a knowledge of spectrographic technique and the examination of materials by methods involving the use of ultra-violet, infra-red, and X-ray apparatus. No one chemist can be expected to be competent to cover such an extensive field adequately, and this difficulty has been met by ensuring that the staffs of

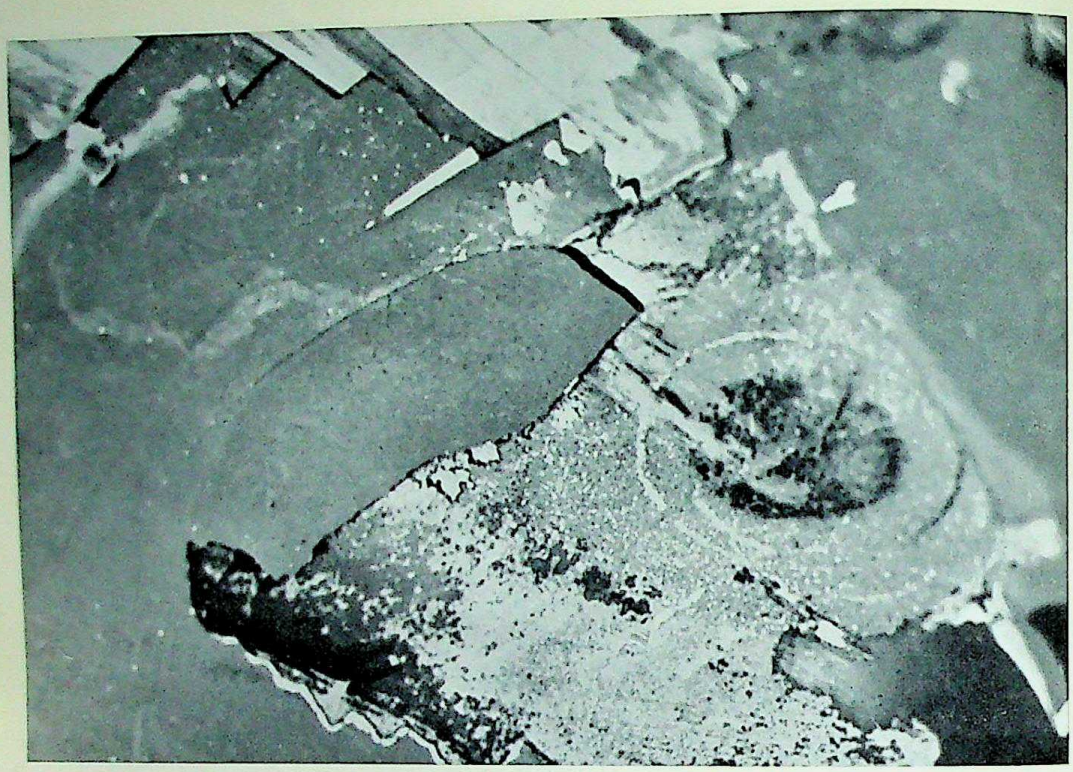
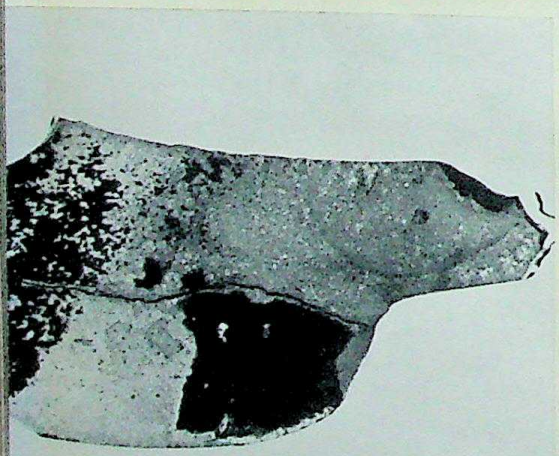


FIGURE 3 – *A piece of detached cellulose, collected from the scene of the same accident, was proved to fit exactly on to the damaged mudguard.*



URE 4 – *In figure 3 it will be seen that there is a light lar mark on the bare metal of the wing. This mark ed to match exactly one found on the under surface of her fragment of cellulose (the upper one in this illustration) d at the scene of the accident.*

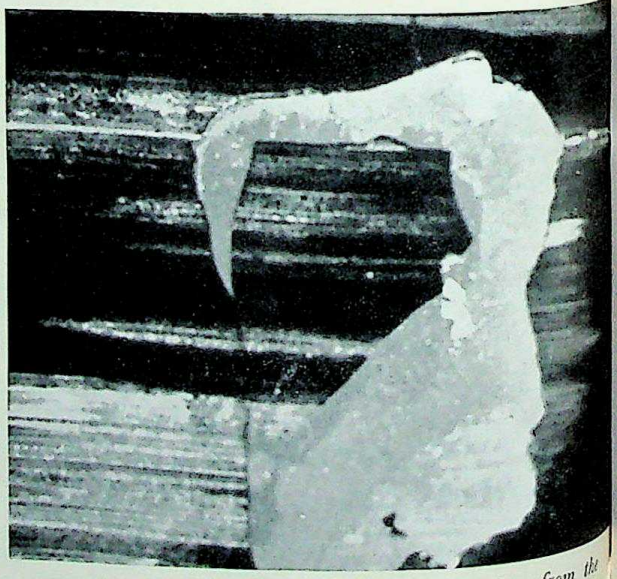


FIGURE 5 – *This flake of cellulose was taken from the clothing of the dead cyclist and is here seen in what was presumed to be its original position on the mudguard. There is a partial fit along one edge, and identification was confirmed by comparison of scratch marks and spectrographic analysis.*

the regional laboratories between them include scientific officers who have special knowledge of tinctorial chemistry, explosives and inflammable materials, poisons and drugs, and such other branches of the subject as are likely to have an application to forensic work.

The range of case material requiring study by the biologist is equally varied and extensive. Typical examples are the identification of wood splinters and sawdust, fragmentary plant and animal remains, the undigested constituents of feeding stuffs, the hairs of various animals, fibres from textiles and cordage, bloodstains, seminal stains, and animal and plant parasites. Work of this character involves the establishment of an extensive collection of authentic specimens, and, frequently, the development of special techniques for purposes of detailed examination and comparison. A wide knowledge of plant and animal morphology, ecology, and taxonomy has been found to provide a most valuable background for forensic work.

Broadly speaking, it may be said that the object of the laboratory study of material submitted by an investigating officer is to connect a suspect, or the vehicle or implements in his possession, with the scene of a crime or the line of approach to or departure from the scene, or to test the accuracy or otherwise of statements made by individuals in whom the officer is interested. The laboratory examination may serve not only to complete a chain of evidence against a suspect, or prove that his story is false or grossly inaccurate, but may equally serve to clear him of suspicion and establish his veracity.

The aim of laboratory investigation must in all cases be impartially to record the factual findings and the reasonable inferences to be drawn from such findings. The findings are always available to the defence, and are supplied to them as a matter of course where they are likely to assist a prisoner. Quite apart from this, an expert engaged by the defence is always given every possible facility, subject to adequate safeguards, for making an independent examination of the material previously submitted to the forensic science laboratory, and of course may report the results of his examination to his clients.

Probably the simplest way of illustrating this aspect of the work of the laboratory is to describe a selection of typical cases, and the examples which follow will, it is hoped, serve that purpose. Both the data resulting from the police side of the investigation and those emerging from the study of material in the laboratory are included.

CASE I

A young married woman was returning from a dance one dark November night to her home on the outskirts of a small town. Some distance from the dance hall she was accosted by a soldier, but ignored him and went on. Immediately afterwards she heard the footsteps of someone coming up behind her, felt an arm thrown roughly round her neck from the back, and received two violent blows, one on the head and one on the shoulder blade. She struck out with a torch she was carrying and heard it hit something metallic which, she thought, was a button or belt buckle. This had the effect of preventing further molestation and she hurried home, where it was found that she had been stabbed on the head and in the back. Medical help was summoned and the police were notified. Beyond the town was an anti-aircraft gun site, and, since a soldier was implicated and since the route to the gun site was that also leading to the girl's home, a check was made on the troops who had been out on short passes that night. It was noticed that one of the men interviewed had several dark and sticky stains, resembling blood, on his clothing, and as his explanation of these was unsatisfactory he was detained. The following morning the scene of the assault was searched, and a small saw-edged knife with a broken blade was recovered. The fragment of blade was also found, and the two parts fitted together accurately and were clearly parts of the same knife. The exhibits submitted to the laboratory were the injured girl's outdoor coat (a greenish rough tweed), her pink rayon blouse, her torch, the soldier's battledress tunic and trousers, and the two parts of the broken knife. There was an obvious stab-cut through the coat and blouse in the region of the right shoulder blade, both of which were bloodstained. The blood, when grouped, proved to belong to Group AB. The stains on the soldier's uniform were due to human blood also belonging to the same group, and were of recent origin. Detailed examination of the knife showed that the tip was bloodstained on both sides, and that the blood was human and belonged to Group AB. The examination of the knife also revealed the presence of a considerable number of fibres caught up in the serrations of the blade. The majority of these were wool fibres of various shades of yellow and brown, with occasional red ones, and could be matched exactly with control fibres taken from the uniform of the suspect. Near the tip of the blade there were, in addition, wool fibres showing detailed agreement with those of the injured girl's coat, and pink viscose fibres matching those of her blouse. It was a reasonable inference from these findings that the knife was the weapon used, and that it had been in the possession of a soldier. Attention was next directed to the suspect's uniform, and on the left sleeve further wool fibres matching those of the girl's coat were found, together with two human head hairs showing detailed agreement with those of

the girl. Here then was a soldier suspect, who had stains of human blood of the same group as that of the injured person on his clothing, with other indications of contact, and who in all probability travelled back to camp along the route taken by her.

A final point which emerged from the laboratory end of the investigation concerned the torch. This showed a linear dent in the nickel casing, and traces of nickel were found along the fracture of that part of the knife blade which was still attached to the handle. It seems highly probable that, when the injured girl struck out with her torch, it hit the knife blade and fractured it, and that the knife was knocked out of the soldier's hand by a second blow, which resulted in the transfer of metal from the torch to the fractured end of the blade. The soldier was charged, tried, found guilty, and sentenced to imprisonment.

CASE 2

The case described below is of some interest in that laboratory examination served to connect two apparently unrelated offences. A saloon car was stolen from a garage in a South Wales town during the hours of darkness. Its loss was discovered almost immediately, and was reported to the police, who circulated its make, colour, registration number, and other relevant details. It was recovered the same night, with an empty petrol tank, on the outskirts of the town, and was dusted for finger-prints with negative results. The officer investigating the theft noticed, however, that there was an appreciable quantity of sawdust on the carpets covering the floor of the car. This was collected and, when examined at the laboratory, proved to be that of Scots Pine (*Pinus sylvestris*), probably the commonest and most abundant kind of sawdust in Great Britain. Its evidential value, taken alone, was therefore poor. There were, however, among the wood fragments numerous small, thin, irregular flakes of brown vegetable matter, which bore a superficial resemblance to broken bits of cigar leaf but which on detailed examination proved to consist of particles of the skin of new potatoes. Further police investigation led to the arrest of two youths, and pine sawdust with the same unusual extraneous plant tissue was recovered from their footwear and trouser turn-ups. This, with other information gathered by the police, served to connect them beyond reasonable doubt with the theft of the car. In the meantime a report was received that a Co-operative shop had been broken into and various articles and cash from the till had been stolen. The floor of the shop was covered with sawdust, which proved to be pine sawdust and contained particles of new potato skin derived from a large serving bin into which the sacks of potatoes were emptied. The accused were, on this evidence, charged with both the shopbreaking and the theft of the car: they pleaded guilty.

CASE 3

Although the poultry thief has always existed, systematic large-scale poultry thefts in Britain are one of the legacies of wartime food shortages. Chickens have always found a ready sale on the black market, especially immediately before Christmas, and expert thieves have developed a high degree of skill in stealing birds with the minimum amount of noise and disturbance. The following case will serve to illustrate some of the ways in which laboratory investigation may be helpful.

A lorry travelling towards London along one of the main roads from the south was stopped after midnight for routine check by a police motor patrol, and was found to have a number of crates of live fowls aboard. The driver, who was accompanied by a second man, mentioned the breed of the fowls, and stated that he had purchased them from a dealer, whose name and address he gave, at a town on the south coast. His driving and road fund licences and insurance certificate were in order, and he was allowed to proceed. Next morning the theft of a hundred and twelve pullets from a south-country breeder was circulated. A lorry had been driven into the field in which the fowls were housed, after the zinc-coated triple barbed wire strands surrounding the field had been cut and bent back. A short strip of rough-surfaced wood about five inches long was the only clue the raiders had left. The dealer from whom the lorry driver stated that he had bought the fowls was located, and proved to be a wholesale fruit and vegetable merchant. He stated that the lorry driver had called at his premises on the afternoon of the previous day and had begged some strips of wood from an empty fruit box for the purpose of mending defective fowl crates. He had not sold him any fowls. Meanwhile the address given by the lorry driver was visited and fowl dung and feathers were collected from the lorry. An almost new pair of stout wire-cutting pliers found on the lorry was also taken into possession. The fowls had vanished, but four were traced, and luckily their crops and gizzards were recovered. These, together with the pliers, the dung and feathers from the lorry, the cut strands of barbed wire, and samples of the food and grit supplied by the farmer to his pullets were submitted to the laboratory. The food consisted of a mixture of wheat, barley, and bran, with a smaller amount of oilcake. The oilcake consisted of a mixture of ground-nut seeds and palm kernel. Traces of all these feeding stuffs—a most unusual combination—were identified in the contents of the crops and in the dung from the lorry. The gizzards contained chopped flint grit agreeing with the sample supplied by the farmer. The piece of wood found in the fowl run was identified by the wholesale fruiterer as from one of his fruit boxes and, finally, in addition to traces of zinc on the blades of the pliers,

many of the slight imperfections in the cutting edges were faithfully reproduced on the cut ends of the strands of barbed wire. Evidence of these findings was given at the trial of the lorry driver and a conviction was recorded.

CASE 4

One of the commonest of the everyday problems posed to the police officers is that resulting from motor accidents in which a pedestrian or cyclist is killed or seriously injured, and in which the offending vehicle fails to stop. The case described in the following note is a typical example of this kind.

A cyclist travelling along a main road in the dusk of an autumn day was knocked down and fatally injured by a motor car which did not stop. The cycle suffered considerable damage, suggesting a severe impact, and this view was confirmed by the discovery of a sidelamp and a number of irregular flakes of black-surfaced cellulose paint at the scene of the accident. The car believed to be the vehicle concerned was traced: its nearside sidelamp was missing, and the nearside front wing was badly scored and dented and had lost a considerable quantity of paint. Some indication of this damage and of that to the cycle is shown in figure 1. The flakes of paint from the scene were collected, and these, the car, and the cycle were brought to the laboratory for detailed examination. The laboratory also received the clothing, footwear, collar, and tie of the deceased cyclist, and samples of his blood and hair. Inspection of the car revealed a number of details which might prove significant. A piece of rag which was wrapped round the leads of the missing sidelamp bore some dark reddish brown stains, and there were several hairs adhering to it. A number of blue fibres were found on the lower edge of the left-hand corner of the windscreen, and these appeared to be of about the same colour as the tie of the dead man.

None of these early finds proved helpful: the reddish brown stains on the rag were paint, the hairs were not human, and the blue fibres were cellulose acetate, while the tie was a blue woollen one. The only significant find in the clothing was a small angular flake of black-surfaced cellulose paint bearing a number of more or less parallel scratches. Careful measurements indicated that the offside pedal of the cycle must have been hit by the front of the car wing, and that the damage to the highest part of the wing had been caused in all likelihood by the metal framework of the saddle. The occurrence of traces of cellulose paint resembling that on the car wing, on both the ball-race cap of the pedal and on the metalwork of the saddle, provided some preliminary check on this interpretation.

It was evident that a detailed study and comparison of the fragments of cellulose paint from the road and from the car were the most promising fields for further study. Figure 2*a* is a photomicrograph of a section taken from a paint fragment removed from the car wing, and figure 2*b* is a photomicrograph of a section from a fragment collected from the road. Although the colours of the sections are not reproduced, the detailed agreement in the thickness and characteristics of the various layers is strikingly clear. The wings had evidently been repainted a number of times, and, in one instance, the addition of further coats of paint before a previous layer had dried had led to a wrinkling of the surface. Spectrographic analysis of the two samples gave identical results.

After exhaustive search, a small paint flake from the road was found, which gave an accurate fit with paint still present on the car wing. This fit is illustrated in figure 3, which also shows a circular mark on the bare metal of the wing immediately to the right. Figure 4 shows the juxtaposition of the above-mentioned flake with a second flake found on the road. Both are photographed from the under side, and part of the circular mark on the wing is shown in reverse on the right side of the upper flake. The evidence that the car under examination had been damaged on the road at a point where the accident had occurred was conclusive.

Attention was next turned to the flake of paint found on the clothing of the dead man, and figure 5 shows an enlarged photograph of this flake in what was assumed to be its original position on the car wing. There is a partial fit along one edge of the fragment, and the close agreement of the scratch marks and scoring of the paint, as well as a spectrographic analysis of the fragment, established beyond reasonable doubt that it had come from the car wing. Analysis of the paint on the metalwork of the saddle and the ball-race cap of the pedal completed the laboratory end of the investigation. The court held that the evidence that the car caused the death of the cyclist was conclusive.

The selection of cases described above, while serving to give some idea of the daily work of a forensic science laboratory, indicates only part of its activities. The members of the scientific staffs may be called upon either for advice to, or to undertake work for, various government departments where it is considered that their specialized knowledge and experience would prove helpful. They must read widely, and be alert to envisage possible applications of new research methods to their problems. They should, and normally do, undertake original work on those parts of their subject in which they are specially interested.

The forensic science laboratory is not for the man who seeks the calm of academic life, or for such as find that steady application in a limited field of study suits their temperament. It provides a career in which hard work, the urge of scientific curiosity, and infinite variety are the chief ingredients and, for the right type of scientist, it is both stimulating and satisfying.

Scientific education in the United States

F. A. PHILBRICK

American teaching of science, in spite of some recent criticism, is directed mainly to practical ends, with the result that relatively slight advances in pure science accompany unsurpassed progress in technology. In American pedagogy new material is presented in separate units, and is sedulously related to familiar experience. Instruction suffers at the lower levels from excessive numbers, but some institutions provide unequalled facilities at graduate level.

Many writers have noted that pragmatism is the chief trait of the American character, whether this is to be attributed to the cast of mind common in emigrants to the New World, or to the conditions of life that they found and developed there. And just as pragmatism has been the dominating philosophy taught in the universities, so in pedagogy has everything been subordinated to immediate and practical ends. In America, the battle for the inclusion of science in the curriculum was easily won. Money for laboratories has been generously provided—it has always been more readily available for buildings than for the men who teach in them—and the visible successes of modern science have given it enormous prestige as an academic subject. So greatly envied is the position of the scientist in the universities that his colleagues in other departments are tempted to describe their own subjects as sciences and themselves as scientists. Thus a historian who emigrates to America may find that he has become a *social scientist*, and in a recent book a psychologist goes so far as to say, 'Scientists study and write about people and the world in which they live'—a definition which seems to include all possible topics.

There are two ways of teaching physical science. One of them begins from the data, either those that were thought significant by early workers (the historical method) or those that are relevant today, and by induction derives the laws of nature. The other begins with the laws, and explains the data as deductions from them or as examples of their application. Whereas the inductive method aims at developing the mind of the student by helping him to organize the data, the deductive method presents him with the data already organized. This second method is universally followed in the United States, whose schools were scarcely touched by the heuristic movement that began in England half a century ago. Thus in an American chemistry course the laws of chemical combination may be presented as deductions from the atomic theory, and such a difficult point as the diatomicity of hydrogen molecules appears as an unaccountable act of intuition.

It is true that there are doubters. Jacques Barzun, in his brilliant and iconoclastic *Teacher in America*, [1] has a chapter on 'The Ivory Lab.' in which he says that science is the worst taught of all subjects. In advocating the historical method of teaching, he claims that the education of students as men and citizens is sacrificed in the colleges to vocational training, and that current methods have produced among the teachers themselves 'many highly trained and absolutely uneducated practitioners.' In his Terry Lectures [2], President Conant of Harvard, possibly the most influential scientist in America, likewise appeals to teachers of science for a new attitude to their subject deriving from some understanding of its history.

These, however, are exceptional views, and the character of American scientific achievement is a consequence of the pragmatic conception of scientific education. The unrivalled successes in technology, and the relatively unimportant contributions to fundamental knowledge, are consequences of the nature of American teaching. Geoffrey Gorer, whose book *The American People* [3] is the most penetrating study since de Tocqueville, is excellent on American science. He points out that basic inventions, whether radar, penicillin, or jet propulsion, are usually foreign, but that improvement, industrial adaptation, and above all diffusion are carried out in America with unique success. 'Make a better mousetrap, and the world will beat a path to your door.' It is improvement that is recommended, not novelty. 'Their attitude towards things,' writes Gorer of the Americans, 'is untroubled by ambiguity, serene and confident, audacious and creative to an extent that no other

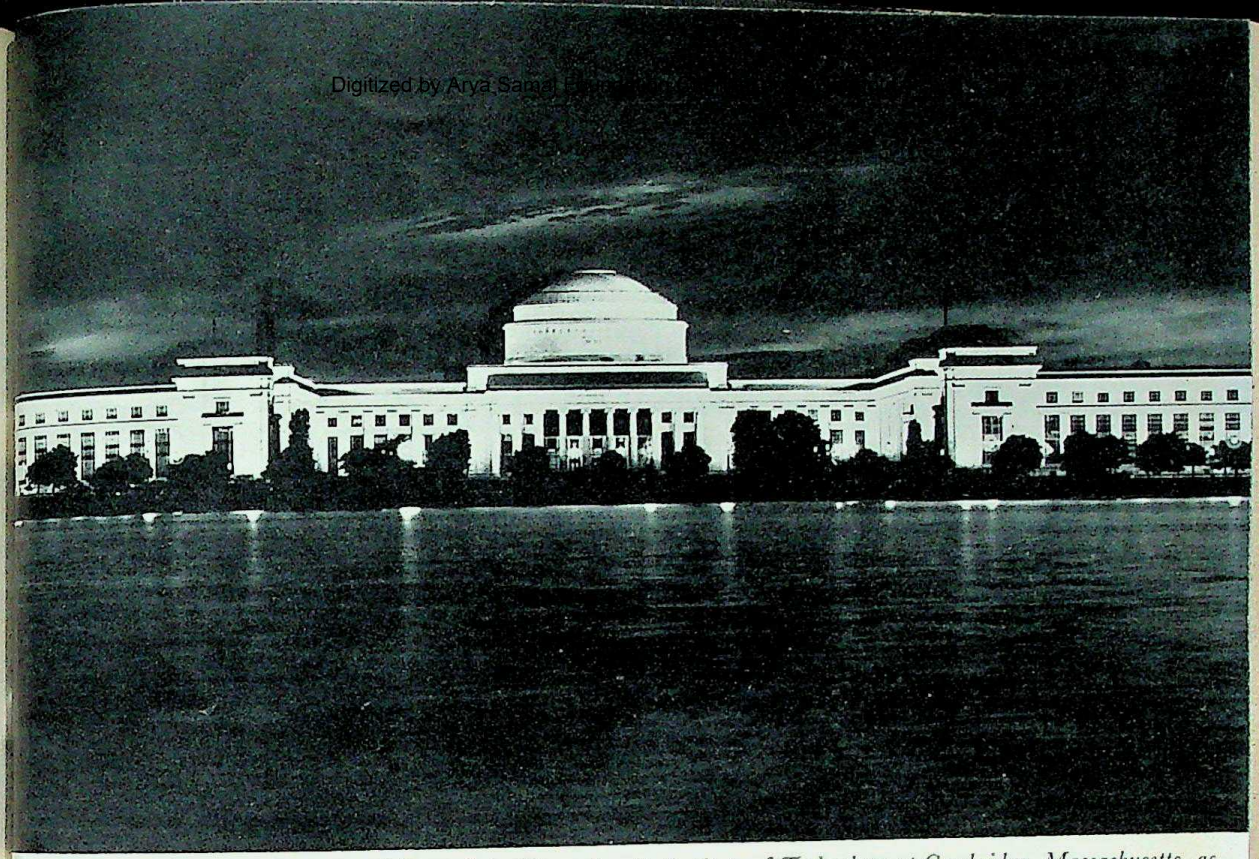


FIGURE 1 – *The main educational buildings of the Massachusetts Institute of Technology at Cambridge, Massachusetts, as they are seen from the Charles river at night.*

FIGURE 2 – *The Museum of Science and Industry at Chicago, on the shore of Lake Michigan, is visited by one and a half million people annually.*

society in the world has seen or imagined. . . . This ingenuity in the exploitation of things has, fairly recently, been given a special term—"know-how"; it is rightly considered peculiarly American.' The admiration accorded to science has in some degree protected science teaching from the encroachments of the athletic coach, the great enemy of education in America—before whom even college presidents are dumb. To the alumni the new laboratory block may be scarcely less an object of pride and interest than the stadium.

Two important pedagogical devices are used in America in presenting to untrained minds the complicated systems of the sciences. The first is a thorough correlation of the discussion with the experience of the student. Any European glancing through an American textbook of elementary science is impressed with the variety of illustrations designed to hold the interest of the reader, and by the pains taken in the text to connect the unfamiliar with the known. If the author is unskilful the device may lead to mere descriptive chitchat, but it is unusual to find an American text in which pedantry or a too rigorously mathematical treatment has kept the exposition above the levels of attention or understanding that can be expected of the reader. The present American eminence in thermodynamics, though perhaps partly derived from the great example of Willard Gibbs, may probably be attributed to the excellence of American textbooks on the subject, which never let the reader forget that this branch of science deals with the real world.

The second pedagogical device is the division of the subject into parts of manageable size. This plan is likewise much in the minds of authors of textbooks, and one may find a discussion of, say, respiration headed in bold type UNIT 17. To gain a rapid mastery of a topic it is undoubtedly wise to study one part of it at a time, and to finish that before going on to the rest, though by this method there may be some loss in total grasp. The efficiency of the method was demonstrated during the war by the success of the service courses which trained men to operate and maintain complicated scientific apparatus. It was perhaps inspired by another typically American technological improvement—mass-production, in which a manufacturing process is divided into separate operations that can be performed on an assembly line.

The fragmentation of the subject-matter of science in American teaching is encouraged by the institutions of the *course* and the *credit*, and by the objective examinations now in vogue. A student takes a number of courses, for instance Botany I or Qualitative Analysis, each lasting a year. When he has successfully completed the course he gets a credit for it, and when he has enough credits he graduates and receives his diploma. Once a particular course has been passed, a student need expect no further examination in its subject-matter, for comprehensive examinations in the whole of some branch of science are, if not unknown in the United States, at least uncommon. It is not surprising, therefore, that the essay-type examination, which tests the candidate's ability to correlate his knowledge of the different parts of a subject, has now been almost displaced by the objective test, consisting of a large number of separate questions often little related to each other.

The undoubted American talent for teamwork and organization relieves a teacher of science of much work that in Britain he would expect to do for himself. In America the duties of a junior instructor may be confined to explaining the textbook, supervising the laboratory work described in the manual, and correcting the objective examinations sent to him in bundles once or twice a month by the head of the department. The class work follows the order laid down in the textbook, which is begun by the teacher and the class on the first page and faithfully followed to the last, each division of the book being completed by all the classes on the same day. In large institutions the textbook, written by the teachers, often circulates for years in an edition produced by photography from the typescript and frequently revised until it is ready for printing and public sale. The system allows little initiative to the teacher, and departmental control is often strict. Instruction under these conditions, though usually efficient, is not stimulating either to teacher or to students, and the more enterprising teachers, if they cannot rise to positions where they have control over their courses, either take administrative work or go into research.

The institutions in which these ideas are put into practice range from the grade schools, through high schools and colleges, to the graduate and professional schools of the universities. The entire population attends at the lowest level, but only a small fraction of it at the highest. Great efforts are made to ensure that the selection for higher training is intellectual as well as financial. In science, for instance, the Westinghouse Corporation conducts an annual search of the high schools to make sure that the boys and girls of greatest promise are sent to college. The early

ecialization usual in England is deplored by merican teachers, and in high school it is most common for any branch of science to be studied r more than two years, one-year courses in ysics, chemistry, or biology being almost uniersal, and astonishingly uniform throughout the untry in content and treatment.

The peculiarly American problem of higher ucation is, however, the presence in the colleges great numbers of students little suited by taste training for the academic life. Inspired by a nerous desire to make higher education as nearly iversal as it can be, the colleges long ago opened eir gates to almost everyone who could pay the es, and the prosperity of the country has multied the number of students. Most American ivate schools send nearly a hundred per cent. of eir alumni to college. The state universities, most entirely maintained by state funds, and ence exposed to political pressures, are in posions of special weakness against the invasion of e incompetent. The hard discipline of the iences, however, has little to attract triflers, so at the departments of science suffer less than ost from standards depressed by excessive numers of mediocre students. But the methods of nstruction have had to be adapted to them. The ecture-demonstrations, often given by the proessor in charge of the course, may be attended by s many as two hundred, and the rest of the teaching is done in the laboratory and in small discussion groups conducted by junior teachers. Attendance at all these is obligatory for every student taking the course, and his progress through the year is followed by the marks that he receives in the frequent objective examinations.

In some colleges specially devoted to science the quality of the work is considerably higher than elsewhere. Chief among these are the Massachusetts Institute of Technology (see figure 1) and the California Institute of Technology, with its remarkable list of Nobel prizewinners from the faculty. These two colleges have high standards of admission, and every June the great industrial corporations are in eager competition for the services of their fortunate graduates. Only a few of the less specialized universities, Harvard among them, are able to offer scientific courses of this quality to undergraduates. If, however, the scientific education of undergraduates in most American colleges is admirable chiefly for the efficiency with which large numbers of indifferent students are given elementary instruction, many of the graduate schools are as good as can be found anywhere. The difficulties that at present beset the academic life in other countries have brought to America brilliant teachers and students from overseas, and a young graduate wishing to do research in the United States is unlucky if he cannot find at least one American university where he can work in perfect conditions and under a scientist of world reputation.

In this brief article only the outline has been traced of scientific education in America. It is impossible to give a fair description either of the great medical schools, or of such unique foundations as the Institute for Advanced Study at Princeton, directed by Robert Oppenheimer and with Albert Einstein on the faculty, or of the extraordinary Museum of Science and Industry at Chicago (see figure 2). After investigating such spectacular exhibits as a full-size working coalmine, a visitor to this museum can witness a demonstration of sensitive apparatus such as the Michelson interferometer. This museum should be seen by all scientific visitors to the United States, who will find here and elsewhere that the traditions of American hospitality are fully shared by her scientists, and that libraries and laboratories are gladly thrown open to scientists from abroad.

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High-polymer molecules in solution

A. R. MILLER

Polymers not only dissolve in a way which cannot be accounted for by the ordinary thermodynamical theory of solution, but the solutions themselves do not even approximately obey the ideal laws. It has thus become necessary to develop a new mathematical theory which will take account of the complex interaction between polymer and solvent. The new theory is generally satisfactory, and such discrepancies as occur may be attributed to changes in the configurational properties of the individual polymer molecules with concentration.

Ideal solutions obey particularly simple laws. The partial pressure of a component of an ideal liquid mixture is directly proportional to the mole fraction of that component. Thus

$$p_i = p_{i,0} N_i \quad \ldots\ldots\ldots\ldots (1)$$

where $p_{i,0}$ is the vapour pressure, at the same temperature, of the pure species i; p_i is its partial pressure; and N_i is its mole fraction in the mixture. The other physical quantities whose values can be derived by thermodynamical argument from the partial pressure, such as the osmotic pressure and the depression of the freezing point, follow equally simple laws. These laws describe the behaviour of low-molecular substances in dilute solution. The quantitative significance of 'dilute' in this connection depends on the components of the mixture which is being examined. For some mixtures, the behaviour will be ideal up to quite high concentrations; for others, the behaviour will be ideal for only very small concentrations.

When a quantitative experimental study is made of solutions which contain high-polymer molecules, very great departures from all these simple laws are observed. It is a fact of common experience that in the presence of a liquid the behaviour of a high polymer, such as natural rubber, is markedly different from that of low-molecular substances. The latter dissolve readily in suitable solvents to a precise maximum concentration. On the other hand, high polymers first swell, imbibing liquid without themselves being dispersed. In a non-solvent nothing further happens, but in true solvents the polymer gradually loses its form and ultimately disperses to form a solution. This behaviour cannot be accounted for by the ordinary thermodynamical theory of solutions.

In the last decade, substantial advances have been made in the mathematical treatment of polymer molecules, and in particular in the development of the theory of solutions in which one of the components is a high polymer. In this particular field these advances have followed from the recognition that, in the language of statistical mechanics, a liquid must be treated as a co-operative assembly. An indication of the implications of this can be given fairly simply. In the simplest applications of statistical mechanics the interactions between the atoms or molecules (described briefly as 'systems') of which the assembly is composed can be neglected. Practically, what is meant by this is that those properties of such assemblies in which we are interested are found to be largely independent of the interactions between the constituent systems. Ideal solutions and perfect gases are among the best-known examples in this category. For instance, the usefulness of the gas scale of temperature lies in the fact that, in the limit of small pressures, the behaviour of gases tends to become independent of the properties of any particular gas—or, as we say, it approaches ideal behaviour. There are other assemblies in which there is a loose coupling between their individual systems, but this interactive coupling has no very profound effect on the properties of the assembly. It can be regarded as a perturbation which modifies the properties of the assembly only slightly. Slightly non-ideal solutions are in this category. There are, however, other assemblies in which the state of any system of the assembly is affected in a fundamental way by the particular states occupied by the other systems of the assembly. In these cases the interactions between the constituent systems of the assembly play a fundamental role, and exercise a dominating influence on the properties of the assembly. Ferromagnetic media, order–disorder transitions in alloys, critical conditions for the condensation of a gas or a vapour on to a solid surface, and solutions of high-polymer molecules are all examples of assemblies of this kind.

Before formulating the physical problem, it is

necessary to adopt a physical model of the assembly which, while being tractable mathematically, provides also a reasonably accurate description of the physical assembly. This we now proceed to do in the case of liquids, considering in particular the way in which our physical model can be used to represent a solution which contains high-polymer molecules. Since it was first realized that X-ray diffraction patterns could be interpreted to provide information about the structure of substances, many liquids have been examined in this way. These studies show that in a liquid there is a high degree of local order between a molecule and its near neighbours, but no long-range order as is found in a crystal. The geometrical relationship between a molecule in a liquid and those molecules in its immediate neighbourhood can be described by an average co-ordination number. There are fluctuations about this average which, while they do not impair the local order between a molecule and its near neighbours, are sufficient to destroy the long-range order. In the light of this picture we can imagine a quasi-crystalline array of sites, in which the geometrical relationship between a site and its closest neighbours is described by an average co-ordination number (which expresses the local order), while there is no regular geometrical relationship between sites at much greater distances.[1] In a liquid the molecules can be pictured as being distributed on such a quasi-crystalline array, this being the simplest picture which accords with the evidence from X-ray diffraction patterns. Thus the simplest useful model of an unassociated liquid is an aggregation of spheres packed together, not tightly, which would represent a crystalline solid, but not very far from tightly. Such a model has less order than a crystalline solid, but it retains a degree of order which is far different from the complete randomness characteristic of a gas. This physical model allows the individual molecules considerable freedom of movement while retaining a high degree of local order.

The extension of this quasi-crystalline model of a liquid to cover the case of liquid mixtures which contain high-polymer molecules is straightforward. A high-polymer molecule consists of a fundamental unit or segment which is repeated a large number of times to form the complete molecule. For example, rubber consists of a large number of isoprene units, each of which is about the same size as, for instance, a benzene or a toluene molecule. The complete 'molecule' of natural rubber consists of many thousands of isoprene units linked together to form a chain. In figure 1 a diagram of an isoprene unit is drawn to show the relative dispositions of the radicals of which it is built up, and also the orientation to one another of successive isoprene units. Natural rubber in the unextended state is fairly adequately represented by a roughly tetrahedral co-ordination of linked subgroups (or segments), with the distance between the centres of mass of neighbouring segments about 4·4 A. This can be compared in size with a benzene molecule, which in the liquid state is roughly an oblate spheroid having major axes of about 6·2 A and a minor axis of about 4·2 A. In considering a physical model of a solution of a high polymer, each solvent molecule can be allocated to one site on the quasi-crystalline array, while to each polymer molecule there must be allotted a large number of sites forming a connected path on the quasi-crystalline array. In fact, each segment of a polymer molecule can be allocated to one site on the quasi-crystalline array, successive segments of a molecule being allocated to closest neighbour sites on the array. Because the sites to which the segments of a polymer molecule are allocated must form a connected path through the array, according as the segments are linked together,

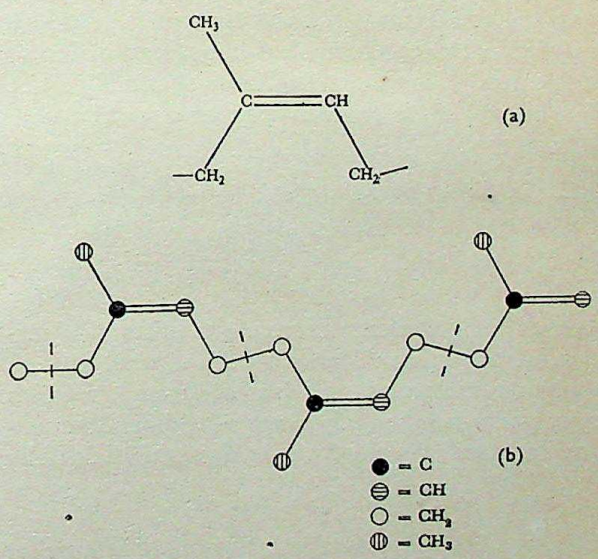

FIGURE 1 – (a) *Isoprene unit.* (b) *The way in which the isoprene units are linked together to form the rubber chain, successive isoprene units being differently orientated. The broken lines indicate the separate isoprene units.*

[1] It should be noted that, in this connection, the word 'order' is used to refer to the geometrical relationship between a small group of sites and not to the mode of occupation of sites on a regular crystalline array, as is the case in considering order–disorder transitions in alloys.

constraints are imposed on the occupation of sites which are near neighbours of one another. Mathematical analysis indicates that these constraints are of the same kind (from the point of view of statistical mechanics) as are introduced by interactions which affect the states of neighbouring molecules. These constraints can be taken into account in examining the physical model which has been described.

The statistical methods which are most appropriate for such a model are those which assume no more than a clearly defined local order between each molecule and its near neighbours. Such methods were first developed in the study of order–disorder phenomena in alloys by Bragg and Williams, by Bethe, and by Kirkwood. It is characteristic of these methods that the occupation of a small group of sites is considered in detail, and average values are used to consider the effect of the occupation of sites outside the group. In this way approximate grand partition functions[1] can be constructed. It is clear that these methods can be applied to a liquid mixture, and it was by using them that an unambiguous expression for the free energy of a high-polymer solvent system was first obtained.

In the first place it is worth while to consider solutions of high polymers in which the energy of mixing is zero. This has the advantage that the effect of the different sizes and shapes of the polymer and the solvent molecules is isolated. This proves to be particularly important, for it appears that the greater part of the divergence of solutions of high polymers from ideal behaviour is due to this cause. The result which was obtained for the free energy of a monomer-polymer system was:

$$\frac{(\Delta A)_{r,1}}{kT} = \tfrac{1}{2}z\{\mathcal{N}_1 + q\mathcal{N}_r\} \log \frac{\mathcal{N}_1 + q\mathcal{N}_r}{\mathcal{N}_1 + r\mathcal{N}_r} - \mathcal{N}_1 \log \frac{\mathcal{N}_1}{\mathcal{N}_1 + r\mathcal{N}_r} - \mathcal{N}_r \log \frac{\mathcal{N}_r}{\mathcal{N}_1 + r\mathcal{N}_r} - \tfrac{1}{2}zq\mathcal{N}_r \log q_r \quad \ldots\ldots\ldots(2)$$

where each polymer molecule consists of r segments, the mixture contains $\mathcal{N}_1$ solvent and $\mathcal{N}_r$ polymer molecules, and q is a parameter which gives the number of closest neighbour contacts made by each polymer molecule and is defined by

$$qz = rz - 2r + 2,$$

where z is the average co-ordination number which specifies the local order. Also $(\Delta A)_{r,1}$ is the free energy of mixing defined by

$$A = A_1 + A_r + (\Delta A)_{r,1}$$

where A, A_r and A_1 are the free energies of the solution, of the pure polymer and pure solvent species respectively. From this expression, the vapour pressure curves can be determined by taking the usual conditions for the thermodynamical equilibrium between a liquid and its vapour. The vapour pressure equations are:

$$\frac{p_1}{p_{1,0}} = \frac{\mathcal{N}_1(\mathcal{N}_1 + r\mathcal{N}_r)^{\frac{1}{2}z-1}}{(\mathcal{N}_1 + q\mathcal{N}_r)^{\frac{1}{2}z}} \quad \ldots\ldots(3)$$

$$\frac{p_r}{p_{r,0}} = \frac{\mathcal{N}_r(\mathcal{N}_1 + r\mathcal{N}_r)^{(\frac{1}{2}z-1)r}}{(\mathcal{N}_1 + q\mathcal{N}_r)^{\frac{1}{2}zq}} \quad \ldots\ldots(4)$$

where p_r and p_1 are the partial pressures of the polymer and the solvent respectively above the solution and $p_{r,0}$ and $p_{1,0}$ are the vapour pressures of the two pure species at the same temperature. The shape of these vapour pressure curves is shown in figure 2. The straight line represents the relation between the vapour pressure and the volume concentration in the solution for a mixture of roughly spherical molecules of equal sizes, and with negligible energy of mixing. The effect of the differences in the sizes and shapes of the molecules of the components is shown by curves (*a*), (*b*) and (*c*), which represent the vapour pressure curves for monomer-dimer, monomer-trimer and monomer-polymer mixtures respectively. It can be seen that even comparatively small differences in the sizes of the molecules of the two components [curves (*a*) and (*b*)] produce appreciable departures from the laws of ideal solutions. When the polymer consists of several thousand segments [curve (*c*)] the departure is very great indeed. The circles in figure 2 represent the experimental points obtained for rubber-benzene mixtures. It is clear that this simple theory, which takes account only of the differences in the sizes and shapes of the molecules of the component species, accounts for the greater part of the departure of polymer-solvent systems from ideal behaviour. Equally good agreement is shown when the theory is compared with the experimental results which have been obtained

[1] A partition function is simply a convenient mathematical way of describing the distribution of the energy over the states of the assembly.

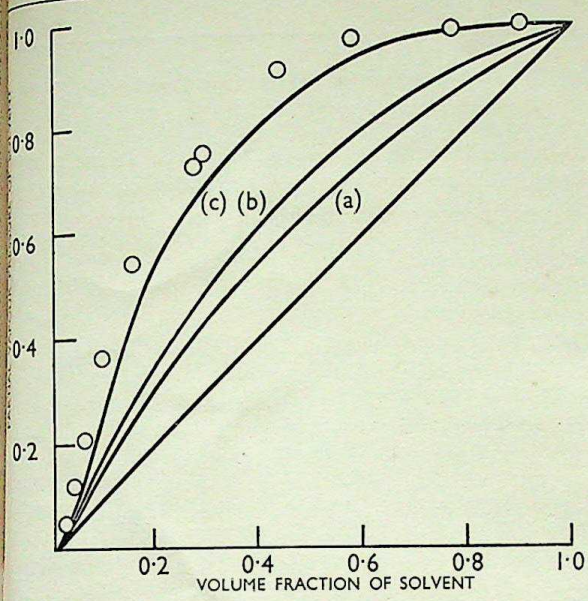

FIGURE 2 – *The partial vapour pressure as a function of the volume concentration of the solvent. The straight line is for an ideal solution, and curves* (a), (b), *and* (c) *respectively are for monomer-dimer, monomer-trimer, and monomer-polymer mixtures. The circles represent the experimental results for rubber-benzene mixtures.*

with other polymer-solvent systems, such as polystyrene-benzene and polystyrene-toluene. The theory has also been able to account for the experimental results which are obtained on the absorption of vapours by high polymers. In this case the molecules of the vapour take the place of the solvent in the liquid mixtures.

More detailed analysis of the experimental results shows that in the region of dilute solution there is some divergence between the theory and the experimental results. This discrepancy cannot be accounted for by the introduction of a non-zero energy of mixing, which has been shown to have a comparatively insignificant effect. Nor is it accounted for by the implicit assumptions of the physical model, which are implied by the use of an average co-ordination number, or the allocation of one site to a benzene (solvent) molecule or to a polymer segment. Neither of these assumptions has any appreciable effect. There is, however, another effect which should be noted. Whereas in solutions of moderate concentration the polymer molecules intertwine and are distributed throughout the liquid phase, in dilute solution they tend to be segregated. Their flexibility about their bonds then makes it possible for the polymer molecules to coil up and to form clusters. This profoundly alters the number of polymer solvent contacts, which in turn affects the variation of the heat of dilution with molar concentration. In the theoretical treatments which have been developed so far, it is tacitly assumed that the configurational properties of the polymer molecules are independent of their concentration in the solution. A study of the configurational properties of polymer molecules as affected by their concentration in solution, and of the consequent effects on the thermodynamical quantities which describe the solution, has yet to be undertaken.

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Book reviews

CHEMOTHERAPY

The Basis of Chemotherapy, *by T. S. and Elizabeth Work. Pp. xx + 435, with numerous line diagrams. Oliver and Boyd, Edinburgh and London.* 1948. 26*s. net.*

In the epilogue to this book the authors claim that chemotherapy as a science has reached the transition stage in which theory has overtaken fact and is beginning to shape the future. How immense already is that body of factual matter and how bewildering is its complexity, with ramifications in many fields of physical and biological science, is probably not appreciated even by those who know something of recent spectacular advances such as sulphonamides, Paludrine, and the various vitamins. The extremely interesting historical introduction will therefore be invaluable for readers who wish to obtain a general survey of the development and present position of chemotherapy. The chapters which follow on cell metabolism, essential metabolites, enzyme inhibition, drug antagonism, drug resistance, and the relation between structure and activity of drugs, provide impartial and well-documented accounts of recent work for those who require more detailed information. In reading the book, which cites in its references nearly a thousand original papers, one is struck by the complexity of the problems, the difficulty of the experimental techniques, and the extreme ingenuity with which the various investigators have sought for solutions or partial solutions. From this wealth of material the authors have extracted the salient features, and have presented them so clearly that their book will be of special value to all who wish to pursue chemotherapeutic studies but whose fundamental training has been in one of the many sciences on which chemotherapy draws. The book is excellently produced, with clear diagrams and easily legible formulae. E. L. HIRST

STREPTOMYCIN

De Koch a Waksman: La Estreptomicina y la Lucha contra el *Mycobacterium tuberculosis, by Florencio Bustinza. Pp. xvi + 269. Espasa-Calpe, S.A., Madrid.* 1948. 120 *ptas.*

The scope of this book is wider than its title indicates. Besides containing a clear and detailed account of the history, manufacture, and medical application of streptomycin, it gives also an excellent survey of antibiosis and antibiotics generally. The literature references are very comprehensive and cover every branch of the subject—medical, pharmaceutical, and chemical. Without in the least indulging in the sensationalism which has characterized much popular writing on this subject, Professor Bustinza has recognized its dramatic side, and has successfully contrived to write this into a precise and scholarly account of streptomycin and other antibiotics. At a time when such great interest is being taken in these substances the appearance of this book will be generally welcomed.

ELECTRONIC THEORY OF ORGANIC CHEMISTRY

The Electronic Theory of Organic Chemistry, *by M. J. S. Dewar. Pp. x + 324. The Clarendon Press, Oxford.* 1949. 30*s. net.*

It is more than ten years since any British chemist has published a book dealing with the electronic mechanisms of organic reactions. The intervening period has seen such important developments as the Hughes-Ingold study of the essential differences between unimolecular and bimolecular reactions, and the detailed application of wave mechanics to the elucidation of structural problems. Since Dr Dewar has considered the main implications of all these advances, Sir Robert Robinson, in a four-page foreword, justly commends the book to students as 'the best available account of modern theories of the mechanism of the reactions of carbon compounds.'

Dr Dewar develops his concepts in terms of molecular orbitals, and shows that this treatment accords with the fundamental theories of Lapworth and Robinson. He has rendered organic chemists a valuable service by breaking away from the static 'resonance state' phraseology of Pauling and Wheland, which has, in several recent American publications, obscured the full implications of the essential differences between the normal and the reacting states of organic compounds.

Unfortunately Dr Dewar has written his book far too hastily. He is candid enough to admit in his preface that he does not accord to individual chemists due priority for their ideas, and he quotes so few references that the source and accuracy of his statements often cannot be checked. Those conversant with the subject will encounter many examples of misquotation of fact, and of misrepresentation of ideas, which seriously detract from the merit of the book as a whole. It is, however, so stimulating to read that it is hoped that a second, carefully corrected, edition will eventually be published.

W. A. WATERS

ELECTRIC DISCHARGE LAMPS

Discharge Lamps for Photography and Projection, *by H. K. Bourne. Pp. xv + 424, with many illustrations and tables. Chapman and Hall, London.* 1948. 36*s. net.*

Electric discharge devices, until recently familiar only to the scientist and the engineer, are now commonplace, even if still incomprehensible, to the ordinary man and woman.

The author of the book under review has considerable qualification and experience as a research worker in this field. The book deals mainly with electric discharge lamps available in England, although there are sections on American fluorescent and flash discharge lamps. The chief electrical and luminous characteristics of discharge lamps are fully described, with emphasis on their photographic and projection use. The title of the book is somewhat misleading and might usefully have included a reference to 'other sources' to cover carbon arcs, which are not discharge lamps in the conventional sense, and incandescent filament lamps.

In this book there is collected together a great deal of information of considerable value to all interested in discharge lamps, whether for photographic purposes or the much more important applications in the field of illuminating engineering. It cannot be said that it is free from fault: the arrangement and presentation of the material are open to criticism. For example, the subject of fluorescence is, for no very good reason, discussed in two different chapters. Again, high-intensity flash-discharge tubes are included in a chapter with photo-flash lamps, which are not strictly speaking electric discharge lamps at all. It is surprising to find no mention of the historically interesting and still important method of spark photography. The use of flashing discharge lamps for photographically recording the finish of races also is not mentioned.

Bibliographical and patent references are given at the end of each chapter. There is a great deal of needless repetition, and much space would have been saved by recording each reference once only at the end of the book. The reproductions are numerous and for the most part good. The publishers are to be congratulated on the high quality of the paper and printing used in this useful book, which should find its way into the hands of all interested in electric discharge lamps. H. G. JENKINS

INDUSTRIAL WASTE WATER

The Treatment and Disposal of Industrial Waste Waters, *by B. A. Southgate. Pp.* 327, *with several line diagrams. His Majesty's Stationery Office, London.* 1948. 12*s.* 6*d.* net.

The purification of sewage and industrial wastes is a vital problem today and the setting up of each new industry brings with it fresh complexities to be overcome. It is thirty-five years since a book on the treatment of industrial waste waters has been published in Britain, and there is no man better fitted to undertake the task than Dr Southgate, Director of Water Pollution, Department of Scientific and Industrial Research. This establishment daily tackles new problems arising from industrial wastes, and carries out research into the treatment of industrial wastes and prevention of water pollution. In addition the author has at his disposal data from papers published in Great Britain and elsewhere, as his department publishes summaries on the treatment of waste waters.

After a discussion of the effect of pollution on the use of water and on fish, chapters are devoted to modern treatment of sewage and general principles of treatment and disposal of industrial waste waters. Then follows the treatment of special industrial liquors. Each industry is first described in simple language to enable the reader to appreciate the processes involved and the trade terms in common use; then follows the main theme of treatment and disposal of waste discharges produced by each process.

Chemical analyses are expressed in parts per 100,000, but it is hoped that in future editions of this book, of which indeed there will be many, the author will reconsider his decision and express the analytical results in parts per million.

Quite apart from its scientific value to a wide field of workers, the author has produced a book which is extremely readable and of absorbing interest, even to those who are not fully conversant with all the specialized processes involved.

E. WINDLE TAYLOR

ELECTRONS AND METALS

Electrons, Atoms, Metals, and Alloys, *by William Hume-Rothery. Pp.* 377, *with numerous half-tones and line illustrations. Louis Cassier Company Limited, London.* 1948. 25*s.* net.

Dr Hume-Rothery recently wrote a book entitled *Atomic Theory for Students of Metallurgy*, and was alarmed to find that this book, written and suitable for the honours student, was largely unintelligible to a number of senior industrial metallurgists. The present work is an attempt to present the modern electron theory of metals to readers who are intelligent and well versed in classical metallurgy but have neither the time for long periods of uninterrupted study nor the mathematical background which the modern student is assumed to possess. Dr Hume-Rothery has cast it in the style of a dialogue between an Older Metallurgist and a Younger Scientist. By this device, and by concentrating on the basic physical principles, he is able to give a very satisfactory account of modern theories in a readable form. It was inevitable that the book should be longer than an orthodox text covering the same ground. The exposition gains greatly from the 165 figures, which are admirably selected, although some of the microphotographs bear no indication of the magnification. Most of the topics treated are covered by the standard books on the electron theory of metals, but the detailed discussion of the factors governing constitutional diagrams will be new to many readers. There is a chapter on plastic deformation, but in general only the equilibrium properties of metals and alloys are considered, and such problems as the kinetics of precipitation are not discussed. F. R. N. NABARRO

SPECTROSCOPY OF FLAMES

Spectroscopy and Combustion Theory, *by A. G. Gaydon. Pp. xii* + 242, *with* 4 *plates. Chapman and Hall, London. 2nd Edition.* 1948. 25*s. net.*

The first edition of this interesting book was published in 1942. It provided a readable account of the principles underlying the application of spectroscopic methods to the study of flames and other kinetic systems, a useful bibliography, and a clear discussion of the contributions made by spectroscopy to the elucidation of certain restricted problems—such as the afterburning of carbon monoxide, on which Dr Gaydon's work has thrown particular light.

A chapter on continuous spectra and the role of atomic oxygen in combustion has now been added, and elsewhere the results of recent experimental work have been included, so that the present edition is longer by some fifty pages than its predecessor, more fully illustrated, and correspondingly more expensive.

This new edition does not warrant any modification of the conclusion—disappointing to a spectroscopist—that the fruits of this method are won hardly, if at all. It seems that the secrets of such complex problems as the burning of hydrocarbons are likely to be unravelled only by joint attacks with all available techniques. To see how little—and how much—may be expected of the spectroscopic contribution one cannot do better than to read this book. R. F. BARROW

FUNDAMENTALS OF PHOTOGRAPHIC THEORY

Fundamentals of Photographic Theory, *by Thomas H. James and George C. Higgins. Pp.* 286. *Chapman and Hall, London.* 1948. 21*s. net.*

The inside of the dust jacket describes this book as 'written for the camera fan as well as for the specialist . . .,' but that must not be taken to mean that it is the usual sort of popular science book about photography. It presupposes a quite extensive knowledge of physics and chemistry on the part of the reader. The authors have wisely limited themselves to discussing the physical and chemical reactions involved in making black-and-white photographs by the use of silver salts. Colour photography is not considered, except incidentally, and then only to the extent of a few paragraphs in the chapter on developer reactions. No attempt has been made to include any discussion of lenses or camera design, which, as the authors explain in the preface, they regard as a separate subject. This decision is one with which few will quarrel, as there have been far too many books on photography which, by trying to cover too much

ground, end by being either too detailed or too superficial. By limiting their terms of reference the authors have avoided these pitfalls and produced a book which is both readable and worth reading. Each chapter is followed by very complete references and there is an excellent index.

As one of the 'camera fans' mentioned on the dust jacket, your reviewer has derived great pleasure and learned a good deal by reading this book. It can certainly be recommended to photographers with a scientific background, and to others who want a general picture sufficiently well documented to enable any particular point to be followed up.

PETER A. LE NEVE FOSTER

COLLOIDS

Colloid Science, *by A. E. Alexander and P. Johnson. 2 vols., pp. 837, with numerous line drawings and diagrams. Oxford University Press, London.* 1949. 60*s. net.*

This book is an outstanding contribution to the literature of colloids, indeed it is probably the first comprehensive treatment of the subject in the light of modern physical chemistry. The first three chapters give an excellent general introduction to the subject; they are followed by thirteen in which different topics are treated thoroughly, both theoretically and experimentally. Some parts of the theory are difficult, but the authors skilfully assume only such prior knowledge as may reasonably be expected of an honours student in chemistry, explaining more advanced theory in the book. Only a few points can be mentioned in a short review; the application of thermodynamics, the theory of strong electrolytes, electrophoresis, and Brownian motion to colloids seem especially good; and the accounts of modern experimental methods and results are excellent and very well selected. There follow three chapters on surfaces, too short to cover the subject properly, but good particularly on modern experimental techniques for studying monolayers. The second volume contains nine descriptive chapters on rather disconnected subjects—dilute sols, gels and pastes, foams, emulsions, colloidal electrolytes, clays and zeolites, proteins, polymers, and membranes. There is a lot of useful information in these chapters, but for a thorough knowledge the larger monographs on some of these topics will be required.

The style is clear and readable, though occasionally reminiscent of rapid notes. The book is one of the very few thorough textbooks on colloid science. It lacks the majestic sweep of Freundlich's *Kapillarchemie*, but its physicochemical treatment is far more modern, and an immense amount of ground is covered.

N. K. ADAM

BRITISH PLANTS

Drawings of British Plants, *by Stella Ross-Craig. Part I, Ranunculaceae, pp. 6 + 44 uncoloured plates; Part II, Berberidaceae, Nymphaeaceae, Papaveraceae, Fumariaceae, pp. 6 + 22 uncoloured plates. G. Bell and Sons Limited, London.* 1948. 6*s. and* 4*s.* 6*d. net respectively.*

These are very pleasant drawings, well printed on good paper. This is saying a good deal, considering modern conditions. Mis Ross-Craig's series includes no descriptive text, but there are a foreword by Sir Edward Salisbury and an introduction by the artist. The illustrations are produced from clear line drawings which show whole plants or parts of plants natural size, accompanied by enlargements of critical features, and sometimes (where the plant is large) by small-scale drawings to show the habit. They quite merit Sir Edward Salisbury's claim that they are 'a happy combination of artistic portraiture and scientific accuracy of detail that should appeal alike to those who use them either as aids to identification, as scientific documents, or for aesthetic pleasure.' It will be a surprise to some readers to learn that, despite the large number of books in existence which deal with the British flora, 'there is still no complete series of drawings of our native flowering plants giving detailed analyses as well as a life-size portrait of each species'; yet such is the case, and it is much to be hoped that the present series will achieve completion. It aims at including all the clearly defined species native to the British Isles, and aliens which have become or are becoming established over a wide area. The parts are rather expensive, but this is made up for by the quality of the paper and printing.

T. A. STEPHENSON

SCIENCE IN FILMS

Science in Films, *edited by Blodwen Lloyd, M.Sc., Ph.D. Pp. 238. Sampson Low, Marston and Company Limited, London.* 1948. 15*s. net.*

The development of the documentary as distinct from the theatrical film during the last twenty years has been a British-led achievement. Films about fact have been made in their thousands, and have been presented in every conceivable way, depending upon the purpose for which they have been made. It is in this choice of the way in which a factual subject has been treated that distinguishes the documentary from the purely scientific film. The documentary tends to be more fanciful in its approach in order to 'put over' fact in an entertaining way; the scientific film treats its subject more dispassionately.

Science in Films, however, covers a range much broader than the purely scientific film. It is a review of the present situation regarding films that have been made with science as the subject matter. As such it is an invaluable book of reference for the scientist and educationalist, the interested layman, and the professional film-maker himself. Chapters by experts review the modern techniques available for the treatment of scientific subjects, including, for example, an excellent chapter on cineradiography. There is, in addition, a section collating information about films on science produced in every country, and about organizations interested in this type of film.

Dr Blodwen Lloyd's book is a reference work that was badly needed in a world where visual aids are being used increasingly for every form of education and information.

J. G. COOK

STRESS ANALYSIS

The Measurement of Stress and Strain in Solids. (*Report of a Conference held in Manchester, 11th, 12th, and 13th July,* 1946.) *Pp. xvi + 114, with 33 illustrations and 8 plates. The Institute of Physics, London.* 1948. 17*s.* 6*d. net.*

This timely volume is a reflection of the growing interest shown in the techniques employed in the measurement of elastic properties—an interest which resulted in the formation in the U.S.A. of a Society for the Study of Experimental Stress Analysis (1942). The result of the Manchester conference has been the formation of a group within the British Institute of Physics devoted to the same end, and the report may be regarded as their inaugural contribution. Some of the papers (such as the late Mr. Eric Jones's paper on physical characteristics of wire resistance strain gauges) are

critical surveys of selected fields. Photoelasticity naturally bulks largely in modern stress analysis, and Mr Fisher's account of some recent photo-elastic developments is a contribution of outstanding interest. Other topics treated are the use of X-rays in the measurement of strains and residual stresses, and high-frequency and acoustic strain gauges. All the topics handled are of great interest to experimenters, but the value of an already valuable volume would be greatly enhanced were it to contain a brief account of the basic principles of photo-elasticity.

The volume is a notable addition to the 'Physics in Industry' series published by the Institute of Physics.

ALLAN FERGUSON

CORROSION OF METALS

Corrosion Handbook, *editor-in-chief Herbert H. Uhlig. Pp.* 1188, *with several half-tone illustrations and line drawings. John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1948. 72*s. net.*

This is not an encyclopaedia, and it is not a handbook in the accepted sense. It falls between the two as a most scholarly presentation of scientific and technical information in the form of separate chapters, each written by a specialist with an international reputation. It very fully treats the theory of corrosion, passivity, and oxidation; the liquid and gaseous corrosion of all the industrial metals and alloys; scaling at high temperatures; and the methods for corrosion protection and testing. There are a glossary, an index, and a large number of tables. The book is practical.

Mechanical effects in corrosion, as exemplified by stress corrosion, corrosion fatigue, and frettage corrosion, are well—if all too briefly—treated. Twenty-seven pages are hardly enough for a series of phenomena which, collectively, are responsible for most service breakdowns.

This book will be welcomed by all industrial research libraries and laboratories, as well as by many practising engineers, chemists, and consultants.

A. J. GOULD

SOIL FERTILITY

Pioneers of Fertility, *by Crichton Porteous. Pp. vii* + 125, *with* 46 *illustrations by Michael Ayrton. Fertiliser Journal Ltd., London.* 1948. 10*s. net.*

Crichton Porteous, novelist of the Adrian Bell school, has made a chronological series of studies of the men who have led us, stage by stage, along the road of expanding soil fertility. Here are Fitzherbert and Tusser; Townshend, Tull, Young, and Coke; Liebig, Lawes, and Gilbert; and many others whose names may be less widely known but whose contributions were no less heroic. 'Heroic' is not an ill-chosen word, for the novelist's instinct in Porteous has emphasized the struggle that almost all of them had to sustain against reaction and prejudice, custom and complacency.

Scientists and practical men follow one another in this delightful procession. Liebig is preceded by John Knight and his son, who left the profitable iron industry to wage a sixty-year reclamation battle with the Exmoor wilderness. And who knows today of John Mechi, a razor-strop magnate who turned to farming as an investment, became a fervent propagandist of new methods, and then lost all he possessed in the first 'cheap food' depression of home agriculture? The theme of the book is the evolution of our modern practices, but there is another theme between its lines —nearly all these men were individualists, fierce or patient. A first-class book for all classes of readers

DONALD P. HOPKINS

SCIENTIFIC INSTRUMENTS

Scientific Instruments II, *edited by H. J. Cooper. Pp.* 306. *Hutchinson's Scientific and Technical Publications, London.* 1948. 30*s. net.*

This well-produced book gives short descriptions, with numerous illustrations and diagrams, of some 150 physical instruments or instrumental systems. They are discussed under seven headings: optical, astronomical and navigational, electrical, electronic, material testing, recording, and miscellaneous, the last containing chapters on ship and aircraft model testing, computing machines, and instrument design. It will be seen that the selection presented is a fairly heterogeneous one, and the editor explains that the intention is to interest the student or scientific worker in some of the instruments in use in fields other than his own, and possibly inspire him thereby, rather than to supply detailed information for the specialist. Some of the chapters will be fairly successful in this aim, provided the reader is comparatively ignorant of the subject; if he has even a nodding acquaintance with it he will probably find that the necessarily rather scanty descriptions tell him little more than he has acquired by general reading, and his interest will be confined to the excellent photographs of modern instruments. There are one or two exceptions to the foregoing, notably the brilliant little essay on computing machines. The editor would have been well advised to omit completely the sketchy account of nuclear disintegration apparatus, however great its topical interest, since much better simple accounts exist. The space occupied by the chapters on electrical measurement and valve circuits would have been more usefully employed in giving references to any of a score of standard works.

B. M. CROWTHER

ZOOLOGICAL DIAGRAMS

Practical Zoological Illustrations, Invertebrates, *by W. S. Bullough. A portfolio of* 32 *cards. Macmillan and Company Limited, London.* 1948. 15*s. net.*

These illustrations, printed on separate cards (37 × 24 cm), are designed to help in the practical examination of those invertebrates that are studied in school and first-year university courses. The author states that he was stimulated into producing them by the inadequacy of many textbook illustrations.

All the figures are semi-diagrammatic and are very fully and clearly labelled; a brief paragraph of practical instructions accompanies each. The author anticipates the criticism that students will be tempted to draw from the figures, instead of from the specimens, by pointing out that it is the instructor's duty to emphasize the importance of individual effort and to teach the proper use of books.

The author first prepared these diagrams for use in his own class, and his students found them so helpful that he now makes them available to others. If properly used they will adequately fulfil their purpose.

L. HARRISON MATTHEWS

PATHOGENIC FUNGI

Biology of Pathogenic Fungi, *edited by Walter J. Nickerson. Pp. xx* + 236. *Chronica Botanica Company, Waltham, Mass., U.S.A.* 1947. $5 *net.*

The reputation of the *Annales Cryptogamici et Phytopathologici* whets the appetite aroused by the title of its latest volume, *Biology of Pathogenic*

Fungi. The first disappointment is in finding that the great majority of pathogenic fungi—those attacking plants and animals—are omitted; the volume deals only with those living on man. The recent work on the nutrition, respiration, and metabolic products of these fungi is covered by Dr Nickerson in a well-balanced 60-page survey. The remaining 150 pages of text have been contributed by twelve authors, who treat in turn of the *Torulopsidoideae*, of chromoblastomycosis, of *Pityrosporum ovale*, of coccidioidomycosis, of Italian 'mycopathology' in 1941–5, of the action of sulphonamides and antibiotics, of the geographic distribution of certain fungus diseases of man, and of the lipids of fungi. Each author starts afresh with his numbering of figures and tables, emphasizing the fact that these contributions are bound together only in the physical sense. It is not without sympathy that one reads the cautious conclusion of Dr J. G. Hopkins' foreword: 'The volume . . . will furnish a useful summary of what has been accomplished in the fields summarized.'

R. W. MARSH

STATISTICS IN INDUSTRY

Statistical Methods in Research and Production (with special reference to the Chemical Industry). *Edited by Owen L. Davies. Pp. xii + 292. Published for Imperial Chemical Industries Limited by Oliver and Boyd, London.* 1947. 28*s. net.*

This volume, prepared by members of the statistical staff of Imperial Chemical Industries Limited, is an important addition to the range of elementary statistical texts. The value to industrial chemists of techniques originally developed for biological data is illustrated by examples from experimentation and routine testing, always with emphasis on the interpretation of the statistical analysis, not merely on mathematical theory or computational procedure. The reader who studies the methodological discussion and the worked examples should have thereafter both understanding of estimation, significance tests, variance and regression analysis, and sampling, and ability to apply the statistical processes for himself. Two chapters on control charts show clearly the natural development of quality control from elementary sampling theory.

The classification of types of regression equation does not seem entirely satisfactory, and the discussion of their errors may increase rather than decrease confusion. An excellent chapter on sampling is marred by description of both stratified random and systematic sampling as *representative sampling*, so obscuring important distinctions in error estimation. These are minor blemishes, however, on a work notable for systematic development, clarity of exposition, and detail of instruction.

D. J. FINNEY

BOOKS TO COME

Bookforecast. *Published monthly by Bibliographia Internationalis Brill, Leiden. Price* 38*s. per annum.*

Only too often one learns of the publication of new books—especially when they are published abroad—long after their first appearance. Although this advance information is available in the advertisements of individual publishers, these are now so numerous—more than 150 publishers of international reputation have already agreed to contribute to this new review—that it is quite impossible to keep oneself informed of all of them. The regular monthly summary provided by *Bookforecast* should prove of considerable value to scientists of all persuasions, as a substantial part of the review is devoted to new books on science, medicine, and technology.

T.R.E.

One Story of Radar, *by A. P. Rowe. Pp.* 206, *with* 7 *plates. Cambridge University Press.* 1948. 8*s.* 6*d. net.*

During the war A. P. Rowe was Chief Superintendent of the Telecommunications Research Establishment, and in this book he has written its history from the beginning. T.R.E. was the original home of radar, and, associated as it was with the R.A.F., which made more use of radar than any other service, it became the largest British organization for research in this field. No small share of the responsibility for the enormous success of T.R.E. must be attributed to the author, whose personality impressed itself so strongly on the establishment. Although not himself a research scientist, Rowe provided a focus for the efforts of the brilliant team he collected, and his strong sense of the proper role of science in war, and of the intimate relationship which should exist between scientist and soldier, did much to direct these efforts into the right channel and to ensure their fruitful application.

As the author points out in his preface, this book does not set out to be a history of radar, but as the history of a vital war establishment it is a fascinating study—the more because in it the author reveals much of himself. It is written in so personal a vein that it will perhaps chiefly interest the thousands who were at some time associated with T.R.E. or worked there; to them especially it will recall something of the atmosphere of this famous establishment which did so much to make victory possible.

J. C. KENDREW

VELOCITY-MODULATED TUBES

Velocity-Modulated Thermionic Tubes, *by A. H. W. Beck. Pp. x* + 180, *with* 56 *diagrams. University Press, Cambridge.* 1948. 15*s. net.*

This book is the fourth of the Modern Radio Technique series, to whose reputation it will add. Like the other books, it describes developments made during the war, largely under conditions of secrecy, and though much of the material has by now been published, a compact and informative *résumé* such as this will prove very useful, both for information and for reference.

A fairly thorough treatment of the theory of energy interchange between electron beam and electromagnetic field forms the backbone of the book, but the author has taken care that the physical action of velocity-modulated tubes is not obscured by the mathematics. The factors governing the practical performance of the various kinds of tubes (of which the klystron and reflex klystron are at the present time the most important) are discussed at length, and the principles of successful design are developed. In this the author has drawn upon his own experience, giving practical examples of design calculations for tubes to meet specific requirements; several tables and graphs of essential data are provided.

Description of practical construction and manufacture is not given, and though there is a chapter in which some details of the design of the component parts and assembly are discussed, no dimensioned diagrams or photographs are included. The book is very clearly printed and easy to read.

B. M. CROWTHER

ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

VOLUME VIII OCTOBER 1949 NUMBER 32

The scientist in society

That science has become one of the most powerful factors in modern life is a generally accepted, and indeed obvious, fact. The proper role of the scientist himself is, however, a point on which there is no general agreement. On the one hand are those diehards who, ignoring the changed circumstances of the outside world, contend that, outside the laboratory, the personal influence of the scientist should be no more than that of any other citizen. On the other hand are extremists who advocate a state verging on a technocracy, in which scientists would have special privileges and a large measure of control. Those who tend towards the latter view are much more vociferous than their more conservative, and much more numerous, colleagues, with the unfortunate result that there is a widespread impression that scientists generally share these views and wish to claim a far larger share in the control of world affairs than they possess at present. It is therefore timely to attempt an assessment of the proper status of the scientist in modern society.

It is necessary first to consider the particular characteristics which distinguish the scientist from the rest of the community. First and foremost, every scientist has been trained in the rational method of thought known as the scientific method. Rational thought is, however, not his monopoly; it is, for example, acquired also by the legal profession as an essential part of its training. Secondly, he assimilates a fund of technical information which is stored in his mind for immediate application to any problems which may arise. Thirdly, his knowledge of, and ability to interpret, the world's scientific and technical literature gives him the possibility of profiting, through libraries, from virtually all the world's accumulated scientific knowledge, though few have such broad understanding that they can readily grasp branches of science far removed from their own.

In a world increasingly dominated by the application of science such a mental armament must necessarily be formidable, and the scientist is indeed indispensable to modern economy. Yet he is but a link in a long chain, and is no more indispensable than other links which support him. There are administrative and economic factors of which the scientist, with his often circumscribed field of interest, usually knows very little. As we survey the world today, it is clear that its difficulties are due as much to intractable administrative and economic problems as to difficult scientific problems. For example, in the new synthetic antimalarial drugs and the new insecticides deadly to the mosquito, the scientist has certainly provided the means of reducing to small proportions the curse of malaria. Yet it is painfully apparent that it will be many decades at least before malaria is eradicated. Again, the need for improved distribution of existing food supplies between the nations is as great as the need for applying science to produce a sufficient total of food for the world's increasing population.

Though there are scientists who believe that such complex human problems could be solved if only they were allowed to apply the methods of science freely, the majority—and the informed lay public—feel that science is of only limited use in the solution of problems largely influenced by emotional and other imponderable factors. None will deny that such problems as the selection and training of industrial workers are ones which deserve the closest study. The successes of operational research have demonstrated the promising possibilities of science in such fields. Yet such human problems are not to be solved by scientists alone; their solution depends equally on the accumulated wisdom of responsible laymen, who interpret such problems in the light of long and varied experience in human relations, and by reasoning

which—until we know vastly more than we do today about the working of the human mind—we must describe as intuitive.

Experience in attempting to forecast the results of the last American presidential election forcibly demonstrated the present fallibility of applying scientific methods to human affairs. It was no isolated example of failure, nor one surprising to those who have carefully considered the possibilities and limitations of the scientific method. In the event, the calculated estimate of the scientist proved no more reliable than that of the intelligent student of affairs.

To say this is not to decry the efforts of the so-called social scientists, or to try to discourage them from further research. That it may ultimately prove possible to find fundamental laws governing human behaviour is not incredible, but it must be accepted as a fact that precise laws of this kind are yet to be discovered; to assume that any have already been established is most dangerous. In this field above all precision is essential and generalizations are worse than useless. In the case of the presidential election, for example, the plea was made that the computors erred only to the extent of a few per cent. This is perfectly true, but so small a difference may determine the way of life of countless millions. The history of all nations shows that under any political system major events can be engineered by small groups—even by individuals. The actions of such exceptional groups or individuals clearly cannot be predicted by any generalizations applicable to men and women collectively.

We are forced to the conclusion that the scientist alone can at present neither predict nor control the future of the community, nor can he alone be of any great practical benefit to it. Accordingly, scientists have no greater claim to privilege and authority than any other professional group. In particular, the suggestion that because of their particular qualifications scientists should adopt a dictatorial attitude in military matters is under present conditions both foolish and perilous. Such limited experience as the world has had of according privilege and power to scientists suggests that they generally respond no differently from their fellows, and the result can easily be the introduction into science of a dogmatism and intolerance which should be wholly foreign to it.

The need today is not for independent action by scientists, but for very much closer collaboration between them and other specialists. One great obstacle to this collaboration is the terminology of science. Scientists necessarily express their ideas in a form often unintelligible to the layman. Furthermore, the very fact that a man takes to scientific research as his life's work is often an indication of strong individualism, which does not make for easy and tolerant collaboration with others. Consequently, collaboration is not too readily effected even when sincerely sought.

It is often suggested that the gap might be bridged by teaching science more widely in schools, but such a suggestion, while not without value, is far from realistic. It is necessary to accept the fact that the modern world is largely controlled by experts—scientific, political, administrative, educational, and so on. Such experts who acquire some elementary scientific knowledge at school will certainly be the better for it, but they will find such knowledge of extremely little value if in later life they have to discuss scientific matters with qualified scientists.

In science, as in other professions, there is unfortunately no short cut to success. To understand science one must study it assiduously. For the world to make the best use of science there seems to be need of numbers of men of a type which today is scarce though not unknown: those who have had a thorough scientific education, but have also had considerable experience in practical affairs. Only through such liaison officers can the scientific and administrative worlds effectively interchange information and ideas—with immense profit to both—for only men with such qualifications are acceptable to both sides. Rightly or wrongly, the scientist commonly has a profound contempt for the layman who ventures into what he considers his own preserves; equally, the man of affairs feels that the secluded life of many scientists ill qualifies them for giving him any useful advice. A liaison officer of the type suggested would have a foot in each camp and could assist both.

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Bacteriology and chemical kinetics

SIR CYRIL HINSHELWOOD

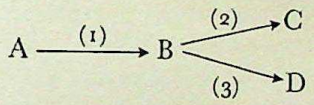
The application of the principles of chemical kinetics to bacteriology has already led to a much fuller comprehension of bacterial activity. Sir Cyril Hinshelwood makes the interesting suggestion that the inheritance of drug resistance and so forth in bacteria may be explained in terms of chemical modifications which persist in the offspring of the modified cells. This conception, he points out, is quite different from the Lamarckian inheritance of acquired characters in general.

It is a commonplace to say that the conventional boundaries of the sciences are rapidly dissolving, and certainly the statement is abundantly illustrated by the relations of chemistry and biology.

Bacteria ought to have a special fascination for chemists, since they perform amazing chemical feats without any of the apparatus in the way of the special organs with which higher plants and animals are provided. They are unicellular, and such internal structure as they possess is so fine-grained and delicate that special methods are needed to reveal it. There are internal inhomogeneities which can be revealed by staining techniques (though these are sometimes suspected of modifying the appearances they are intended to reveal), or by phase-contrast microscopy. Some parts of the cell material are fairly generally supposed to be analogous to the nuclei of other cells, and to undergo cyclical changes in distribution. Bacteria, however, do not possess the obvious chromosomes of some cells, and there is no generally accepted evidence of a sexual process of reproduction.

Many of them grow when provided with such simple constituents as glycerol, ammonia, and a few inorganic salts. In the space of about half an hour each cell synthesizes all the necessary proteins, nucleic acids, and other macro-molecular compounds required to reduplicate itself. It then divides into two by a process which may to some extent be accelerated or retarded independently of the actual rate of increase of mass, so that changes of cell size occur. The growth process must involve a series of polycondensation reactions, in the consideration of which chemical kinetics surely has something to say.

Bacteria indeed show many phenomena which excite the interest of the physical chemist. It might at first sight be supposed that the sequences and combinations of chemical reactions taking place in them would be too complex to be sorted out in the kind of way in which physical chemists try to analyse simpler systems. This, however, is not so. General propositions about groups of linked chemical reactions can be correlated with general facts about bacterial behaviour. An example will perhaps make this point clearer. Suppose we have a system of competing reactions on the following general plan:



Acceleration of process (2) will deplete the supply of B and therefore adversely influence the rate of process (3).

The following group of observations does in fact seem to be based upon the kinetics of just such sets of competing reactions:

(*a*) Certain cells will multiply readily in presence of sodium nitrate as a source of nitrogen. If an ammonium salt is added to the medium it is at once utilized, and reduction of the nitrate ceases abruptly.

(*b*) Coliform bacteria normally use atmospheric oxygen. They can adjust their economy to derive the oxygen from nitrates. If, however, a culture which is reducing nitrate is suddenly aerated, reduction of the nitrate stops. Evidently the oxygen removes an intermediate which is required for reaction with the nitrate. Further adjustments may, however, occur slowly and bring about the result that nitrate may be reduced even in presence of oxygen.

(*c*) Some bacteria will grow both aerobically and anaerobically, and these show the well-known Pasteur effect. Anaerobically, they bring about disproportionations of carbon compounds. In presence of oxygen, not only does profound oxidative breakdown occur but the disproportionation reactions are actually inhibited. Agents which would cause reduction of the carbon substrate are

removed too rapidly by oxygen to exert the effects which they could exert in its absence. The point about these phenomena is this: they are evidently explicable in terms of an interference with one reaction by a competing reaction which consumes a common intermediate at so great a rate that its rival is inhibited.

Now there should be other groups of facts which also can be correlated in terms of what might be called general propositions in chemical kinetics. The complexity of the machinery of cell growth being essentially chemical rather than mechanical, it is evident that the vast series of consecutive and competing reactions can be interfered with and modified in numerous kinds of way. One way which is obviously possible, and which strikes the chemist as being important, is that the relative velocities in a series of consecutive reactions can be changed. The peculiar importance of this is as follows.

When a cell grows and reproduces itself, there occurs an elaborate series of consecutive reactions leading to the synthesis of all the various parts of the cell material in what, under constant conditions, are constant proportions. Every part of the material, since it is in fact reduplicated at each cell division, is effectively autosynthetic, though the autosynthetic character must depend upon the mutual interaction of groups of enzymes and cannot be an inherent property of all enzymatic material. Growth depends upon a series of enzyme processes in which the products of one process constitute the raw materials for the next, and are thus active intermediates in a sort of continuous production line.

When the conditions of growth are changed, for example by the provision of a new source of carbon or nitrogen or by the addition of drugs to the medium, the relative velocities in this chain of processes may very well be rather profoundly modified. If this is so, some parts of the cell material may be synthesized more rapidly than others, and the actual proportions in which the various constituents are present when the moment comes for division will be changed. The result of the division process will be a cell in which the chemical and material balance is different.

This elementary notion at once attracts the attention of the chemist to the extraordinary adaptive phenomena exhibited by bacteria.

Bacteria are extremely variable, though it must be emphasized that the variability manifests itself only within definite limits. One bacterium never changes into another of completely different type, but within a certain amplitude its properties vary very considerably. Some of the types of variability will be briefly indicated.

(*a*) The cells may normally refuse to utilize a given carbon substrate, but after remaining in contact with it for a time they may grow, at first slowly, and then at an increasing rate, until finally they use it with optimum efficiency. For example, *Bact. coli mutabile*, which could grow immediately with glucose as carbon source, waits several days before it will touch lactose, which it then consumes. After a little 'training' it continues to consume lactose as well as it could glucose.

(*b*) Bacteria placed in presence of inhibitory substances, at concentrations just insufficient to suppress growth entirely, multiply with extreme difficulty at first, but after a time acquire the power of growing as though the toxic agents were not present at all. They are said to have acquired drug resistance.

(*c*) When they have been trained to use new sources of material or to resist drugs, bacteria not infrequently show limited but quite definite changes in biochemical properties, such as enzyme activity in particular directions.

(*d*) When exposed to short-wave radiation, such as ultra-violet light, bacteria which are not killed outright may show changed properties. The change is usually such that the cell has lost some of its initial chemical potentialities. For example, whereas initial growth might have occurred quite readily with ammonium salts as the sole source of nitrogen, after the irradiation the use of this simple source for synthesis becomes very difficult, although growth with utilization of suitable amino-acids remains easy. Evidently the ultra-violet light damages some part of the synthetic mechanism. It is to be noted, however, that this can repair itself automatically in the course of a process whereby the cells are left in contact with a medium containing ammonium salts, which they become re-trained to utilize.

It is attractive to attempt to make a working hypothesis in which phenomena such as these are interpreted by applications of chemical kinetics. There is not space to discuss the matter in any detail, but a simple example of what is meant may be quoted.

One very natural way in which a drug can retard part of the autosynthesis is to cut off the supply of an active intermediate by interfering with the operation of the enzyme which provides it. Now it is reasonable to imagine that there are certain essential parts of the cell structure, and

that until all these have been built up in some critical amount there will be no cell division. If the growth of some essential part is inhibited by the action of the drug, and if division waits until this part attains its normal critical size, then it is clear that in the meantime other parts of the cell, not inhibited by the drug, will often be built up in more than the normal amount. These 'expanded enzymes' include those which provide the active intermediates for the systems inhibited by the drug. The active intermediates can now be formed in more than the normal concentration, and will thus be able to antagonize the action of the drug on the inhibited enzymes.

Examination of the differential equations for the consecutive reactions occurring in a very simple model based upon the above idea shows that the enzyme proportions in the cell may continue to change until the growth rate attains the normal value in the drug-free medium. This constitutes an automatic development of drug adaptation.

In a very crude way this notion is illustrated in the diagram. In row 1 (*a*) and (*b*) are two enzyme systems which increase in step until there is enough of each for the cell to divide as indicated. The intensity of the shading represents the concentration of the active intermediate which (*a*) produces and (*b*) utilizes. In row 2 the inhibitory action of the drug is supposed to be exercised on the production of the intermediate by (*a*). There is a reduced concentration, so that by the time (*a*) has attained the state normally corresponding to cell division (*b*) is lagging behind. Division waits until (*b*) has reached the appropriate state (third diagram of second row). By this time (*a*) is present in so much greater amount than normal that the concentration of the intermediate has been restored. Division then results, with the production of two cells each containing subnormal amounts of (*b*). The third row represents the behaviour of the adapted cell in presence of the drug. The increased amount of (*a*) gives an extra supply of intermediate which can compete effectively with the drug and allow the normal growth of (*b*). This picture is of course grossly oversimplified, but it seems hard to believe that phenomena of this general kind do not occur, and that they do not have their significance in adaptive processes.

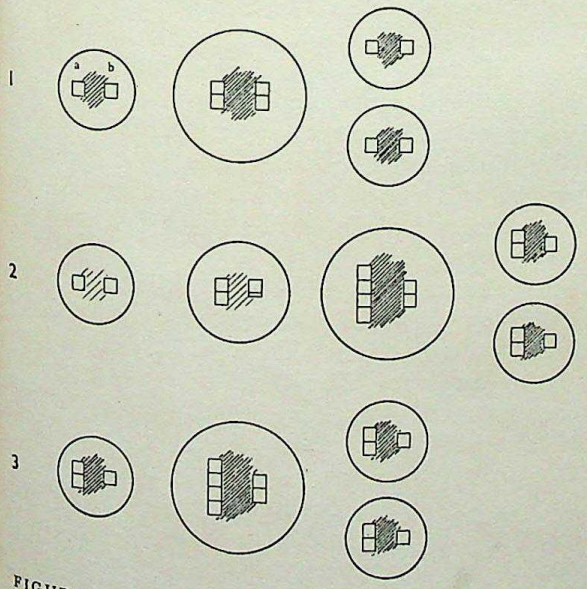


FIGURE 1 – *Diagram to illustrate the automatic development of drug adaptation.*

Indeed, a rather more general study of the differential equations of consecutive reactions by which a series of enzyme systems is built up in a co-ordinated manner shows that the system as a whole will (on some quite simple and plausible assumptions) often have the property of so adjusting the proportions of its various parts that an optimum overall growth-rate will be established. This clearly has considerable significance in connexion with the adaptation of bacteria to growth under new conditions generally, and in particular with the utilization of fresh sources of material.

The assumptions underlying these ideas are not very specific or very arbitrary. Indeed they are little more than formulations of obvious experimental facts. Bacterial cells can grow by the utilization of the most varied substances. According, therefore, to the medium in which they multiply they must utilize different reaction routes. The combinations of possible routes constitute a kind of railway network. Some parts of the possible network will be slow, some rapid. For the total complex series of simultaneous and successive chemical changes there will be, for a given medium, one route through the network which can be traversed more rapidly than any other. This quick route will be different for different media. This is the first principle.

The second principle is as follows. When the cells grow, every single enzyme system is reproduced. ('Enzyme system' is here used in the widest sense to include what are variously called enzyme precursors, plasmogenes, co-enzymes, and so on.) It is very clear that the reproduction of the enzyme systems is closely linked with their functioning, since growth cannot occur without the elaborate functioning of all. Therefore, when growth by a

given chemical route occurs, it is almost certain to be accompanied by a preferential building up of precisely those parts of the enzyme system which are most in use. There is an obvious physical hypothesis about this, namely that the synthesis of proteins and other compounds is guided by existing structures in a manner analogous to crystal growth, but, as far as kinetic consequences are concerned, one can regard the correlation of function and autosynthesis independently of any detailed picture.

Such ideas have been criticized as lacking demonstrative significance. The criticism misunderstands the purpose of the argument, which is not to explain autosynthesis, but to show that the fact of autosynthesis demands changes in enzyme proportions according to the circumstances of growth. These changes in proportions would have the clearest connexion with adaptive processes. If the utilization of a new substrate demands the functioning of an enzyme present initially in minute proportion, then growth will be initially difficult. But there seems very good reason to believe that, if this enzyme can be reproduced at all, then it will increase in proportion as expansion of the total material takes place in the new medium.

The hypothesis about adaptation just discussed envisages a change in the proportions of different kinds of enzyme material. Other kinds of changes which must be considered are those in the actual composition of the macro-molecular constituents themselves, and in the mode of folding and disposition of their structures. These factors are clearly subject to influence by alteration of substrates and so on, in a way to which kinetic considerations are relevant.

It might have been supposed that the construction of models of this kind would be regarded as reasonable hypotheses of the chemist, to be judged as helpful or unhelpful and pursued or discouraged accordingly. But here we run into stormy weather. The changes which accompany the development of drug resistance, or the acquisition by the cells of the capacity to utilize a new source of material, are often transmissible to the progeny formed by the division of the original cells. This has led some people to take the following standpoint. Drug resistance, to take a typical example, is, they say, an acquired character, and therefore could not possibly be inherited. To suppose that it could, would be 'Lamarckian' and therefore heretical in the extreme, rendering those who entertained such a chemical working hypothesis about bacterial affairs liable to condemnation without trial.

Let us examine briefly the logic of this position. Lamarck supposed that changes produced in an entire animal by its mode of life could be transmitted to the offspring. For example, the children of a blacksmith might have unusually muscular arms.

Of course they do not, and the reason is sufficiently clear. The changes brought about in the blacksmith's arms do not affect the hereditary material. In the same way, even the blacksmith's addiction to a drug would be rather unlikely to affect the genes he transmitted. If, however, something were done to him which actively changed the germ plasm, then inheritable effects might well occur. The failure of what can legitimately be called the Lamarckian idea is clearly due to two things: first, that in complex organisms environmental influences, chemical or otherwise, are extremely unlikely to have a chance to act upon the germ plasm, and secondly, even if they do, they are still sufficiently unlikely to do anything significant to it, between killing it outright and leaving it alone. Thus it would appear that environmental effects on heredity might in principle appear in rare cases, but that the chance of producing any by conscious effort is very small. What the uncontrolled effects of cosmic rays and the like may be no one at the moment is really in a position to say.

With unicellular organisms, however, the position is surely very different. As we have seen, changes in the proportions and even in the structure of the self-duplicating material are possible in principle as a result of changed relative reaction rates. The cell produces its progeny by simple fission, so the considerations which explain why acquired characters of intact organisms are not passed on have no weight. Painting the outside of the building where the bank notes are printed will not affect the appearance of these notes: pouring nitric acid on to the printing press itself may well do so.

But the rejection of illogical prejudices against a working hypothesis does not in the least establish that hypothesis. There is a well defined alternative view about adaptive changes in bacteria themselves: namely, that of the selection of chance variants. This will now be considered. The point I have wanted to make first, however, is that the choice between hypotheses depends upon detailed and rather intricate technicalities, and is not in any way assisted by slogans and labels, whether applied in condemnation or in approval.

Having made this point as clear as may be, let us examine the pattern of a typical adaptive change, namely the development of drug resistance.

On culture of the cells in presence of graded amounts of the drug the resistance develops rapidly. In general, it does not appear except in so far as new material is actually synthesized. As soon as the cells are able to grow normally in presence of the drug they are said to be trained. When the training is just complete it is unstable, in the sense that if the bacteria are returned to a drug-free medium and allowed to multiply in it for a season they revert and lose their resistance. If, however, they are trained by being allowed to multiply for a much more prolonged period in presence of the drug, then the adaptation becomes stably impressed upon them, and they will retain their resistance during many generations of growth in the complete absence of drug to keep them, as it were, in practice. Actually, it is more correct to speak of metastability than of stability, since under appropriate treatment (growth in various unusual circumstances) they will lose their resistance and revert. For example, certain cells trained to resist sulphonamides lose their adaptation when grown in presence of acridine derivatives.

If these facts are interpreted in terms of selection, then there are two possibilities. The first is that the original strain was heterogeneous, and contained inherently drug-resistant types which multiply differentially in presence of the drug. This can be definitely disproved, since all kinds of adaptive phenomena manifest themselves with strains which were originally derived from single cells. The second is that chance mutations are continually occurring to produce strains with every conceivable type of property, and that the most suitable are selected out in the course of the training. Unstable training would be characteristic of an impure resistant strain, stable training would be attained when the resistant strain had been purified by long enough continued selection. Ultimate reversion under abnormal conditions would have to be ascribed to a 'back mutation.'

From here the argument, I think, develops along lines which will not be very welcome to those who like to manufacture clear-cut ideological issues. We begin by asking in what the chance mutations consist. Crude actions such as the chemical effects of cosmic rays are not very satisfactory to postulate, since innumerable forms of adaptation occur, and many kinds can be superposed one upon the other. Thus the mutational changes must be, as it were, of a fine-grained and subtle texture. Permutations and combinations of not too small numbers of genes would provide an answer, but where are these to be found, and how are they to be redistributed, in a non-sexual unicellular organism with only fine-grained structure? It does not seem too much to suppose that a quite considerable proportion of the bacterial mass itself possesses genic character, nor does it seem out of the question that the 'genic' character of a bacterial cell might be a function of the quantitative proportions of its components, or of the precise chemical composition of its macromolecules, or of the folding of its proteins, all or any of these factors being closely related to the configuration of its nucleic acids.

All that the chemical theory suggests is that changes in these are forced upon the cell by changed relative reaction rates prevailing when autosynthesis occurs under changed conditions, and that in unicellular organisms not everything is governed by purely combinatory processes. Even here, of course, it may be said that a chemical change is itself only a combinatory change of atoms, so that in the last resort the question at issue is one of scale only. In a sexually reproducing organism, where genes are carried in chromosomes, one can see that the grosser combinatory changes are of major importance, and that chemical changes in genic material likely to be rare. Bacteria lie at the other extreme of a spectrum. It is difficult to see how gross combinatory changes can be of outstanding importance except on a scale where they are describable in the terms used above. Chance development of drug resistance may of course occur: it seems more probable that the response develops as a result of the changed reaction rates in the way outlined earlier. Indeed, if this possibility is denied, it would seem incumbent upon us to find a positive reason why so simple and obvious a mechanism should be excluded.

There remains the problem of why chemically induced changes should be stable in the absence of active disturbance. Two factors would contribute. First, the pattern of existing material in certain key parts of the cell may well guide the deposition of fresh material in a manner somewhat analogous to the growth of crystals. Secondly, if an enzyme has increased in amount to produce, say, excess of some intermediate to combat the action of an inhibitor, when the latter has been removed this excess of intermediate does not need

to provoke a reversion, as may easily be shown by a simple quantitative calculation.

What has been said has tended to blur the sharp distinction between the mutational and the adaptive view of cell changes, and this I believe is right. But there is one respect in which, at first sight at least, a rather important difference exists between the selection view and the view that adaptive response may occur as a result of changed reaction rates. In one case the change is initiated in very few cells, which presently outgrow all the rest; in the other case it affects the bulk of the cell population more or less uniformly. Here again, the final answer will probably prove to be that there are types of behaviour varying between two extremes. In some cases, however, it seems definite enough that the modification occurs more or less equally in all the cells. For one thing, changes in a property of a bacterial population do in fact sometimes occur under conditions where it can be directly shown that the two extreme 'types' have exactly the same growth rate and so would not suffer differential increase.

Another kind of evidence is illustrated by an example which can be given in slightly more detail. Sometimes bacteria placed in contact with a new sugar, such as lactose, refuse to grow for several days, after which they will multiply well enough. The two views are: (1) The original population contained only a very minute fraction of variants capable of growing at all and the delay represents the time which they require to multiply up to a number detectable in comparison with the large number which do not multiply. (2) They all take a long time over growth in the first instance because they lack the necessary intermediates to utilize the unaccustomed source. The delay represents the time during which enzyme systems not normally much used elaborate these intermediates. In the course of the subsequent growth by the new mechanism these enzymes undergo an automatic expansion whereby training occurs. In point of fact, it has been shown that, in some cases at least, practically every cell of the original sample plated out on the new medium (in a solid form to allow counting of colonies) does in fact grow after the lapse of the requisite time, and the same conclusion may be reached by another technique for liquid media.

Suppose dilutions down to 10^{-8} of a given culture grow on transfer to a fresh glucose medium. The last dilution to give positive results may be presumed to contain about one single living cell. Suppose further that only 1 in 10^5 of the original cells are, say, '*d*-arabinose variants.' The last dilution to show growth on transfer to *d*-arabinose would be about 10^{-3}. On the other hand, if all the original cells were capable of adaptation, then positive results would be found down to the 10^{-8} dilution, but growth would require much longer. In some cases at least the second possibility is realized.

Thus in certain examples the direct adaptation does occur, and does apparently represent the establishment of a new chemical growth-sequence.

Once again, however, apparently sharp issues become blurred. When the new growth-sequence is established, certain enzymes originally present in small amount per cell increase relatively to the others. This might in a sense be called an internal selection.

In some cases, no doubt the required enzymes or modified genic material might be confined to a few fortunate cells. There would then be external selection, but in both cases a relative change of proportions occur.

There are very many other ways in which chemical working hypotheses may possibly throw light upon cell working: the study of oxidation-reduction relationships in connexion with aerobic and anaerobic growth rates, the study of substances which accelerate or retard division, and innumerable other matters. But the chemist must realize that he uses very crude tentative models of very complex affairs and should be modest in his conclusions, while perhaps some biologists have need to discard a few prejudices.

Autumn colours

W. H. PEARSALL

Autumn, the 'season of mists and mellow fruitfulness,' is marked by a vivid display of leaf-colour which goes far to allay regrets for the summer that is past. Professor Pearsall explains how and why the autumnal colours are developed; he shows that the changes are intimately connected with the seasonal life-cycle, and relates them to other colour-changes in plants.

The autumn colours of leaves mark the end of the annual growth-cycle of the leaves that show them. Each leaf has passed through three stages: one in spring, when it was engaged in building up its own living material and structure; a second and longer one through the summer, during which it was manufacturing foods for the rest of the plant; and a third stage marked by autumn colorations, in which valuable materials present in the leaves are being removed for storage.

The processes leading to the appearance of the autumnal colours are obviously associated with the death of the leaf, and it is not a difficult matter to show that they are also associated with the evacuation of materials from the leaf, particularly of those substances which are, in fact, valuable for the initiation of further growth in the following spring. It is not necessary, however, to suppose that this is purposive, but merely that the balance between various processes so changes that this is the result. During most of the summer, the removal of such substances as protein and starch from the leaf on the whole balances the rate at which these materials are manufactured, so that the overall changes are small. As the leaf becomes old, however, the rates of synthesis fall off while the breakdown processes are accelerated, a natural internal change that is much accelerated by the less favourable conditions in autumn. It leads to the production of soluble substances like sugars, which are easily transported from the leaf elsewhere.

It is evident from superficial observations that the changes in colour generally follow a definite order. The first sign of change is often that the green leaf shows a tendency to become red (figure 9). There may, at this stage, be no signs of yellowing (figure 12). In many plants, however, reddening is associated at a slightly later stage with the development of the normal yellow colour (figure 7). In any case, a stage is reached at which yellow is one of the predominant colours (figure 1), and shortly after this the leaf becomes brown (figure 2). This final stage is associated with the death of the cells and with the drying of the tissues as a whole.

There are many leaves, however, which do not produce a red colour. The beech (*Fagus sylvatica*, figure 2), the plane-tree of London squares (*Platanus acerifolia*, figure 11), and the maidenhair-tree (figure 6), as well as native English Oaks (*Quercus robur* and *Q. petraia*) are all species of this type. The yellow colours occur in all plants to a more or less marked degree. They are most evident in trees of the temperate climates simply because these are strongly seasonal. In tropical forests, where the climate varies little with the seasons, the trees show both leaf-growth and leaf-fall at almost any time. Similarly evergreens, like pines and firs, are continually producing and losing leaves, though each leaf may stay on the plant for two or three years. As only a few leaves change colour at any one time, the effects are not noticeable. The few trees of this group, the Gymnosperms, that produce annual crops of leaves each spring show well-marked autumnal colour changes (*cf.* figure 6).

The actual sequence of events thus depends upon the capacity of leaves of different species of plants to produce colours. The colours belong to three main groups. The normal green colour of a leaf is due to the presence of *chlorophylls*, complex green pigments containing the metal magnesium, which are intimately concerned with the normal synthetic functions of the leaf. Besides these green pigments, however, a leaf also normally contains two sorts of yellow pigment known as *xanthophylls* and *carotenes*. The former are also present in many yellow flowers, such as daffodils, while the latter are mainly responsible for the colour of carrot roots. All these green and yellow pigments are insoluble in water and can normally be removed from the leaves only by using solvents such as acetone, alcohols, or chloroform. In addition to these pigments, some plants may also contain

FIGURE 1 – Liriodendron tulipifera (*Tulip tree*).

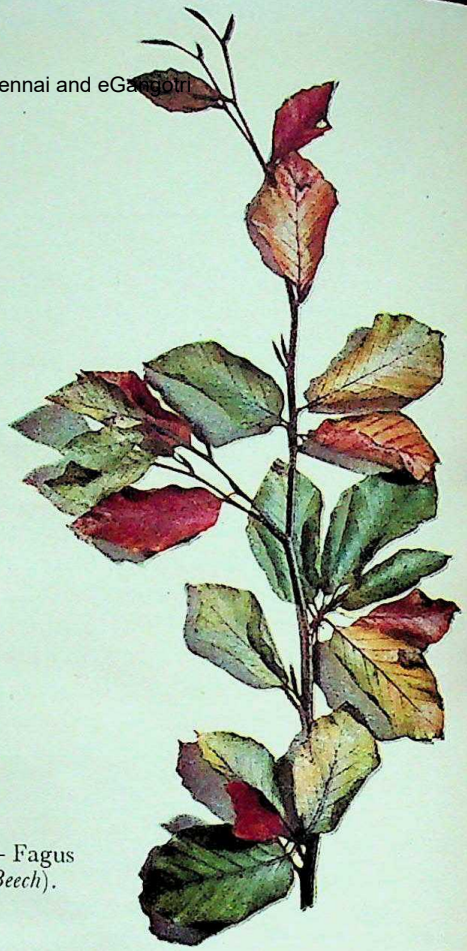


FIGURE 2 – Fagus sylvatica (*Beech*).

FIGURE 3 – Prunus serrulata.

FIGURE 4 – Nyssa sylvatica

FIGURE 5 –
Sorbus domestica.

FIGURE 6 – Ginkgo
biloba (*Maidenhair-tree*).

RE 7 –
ia persica.

RE 4 –
ylvatica

FIGURE 8 – Sc
aria (*White Bea*

FIGURE 9 – Acer nicoense—*Japan.*

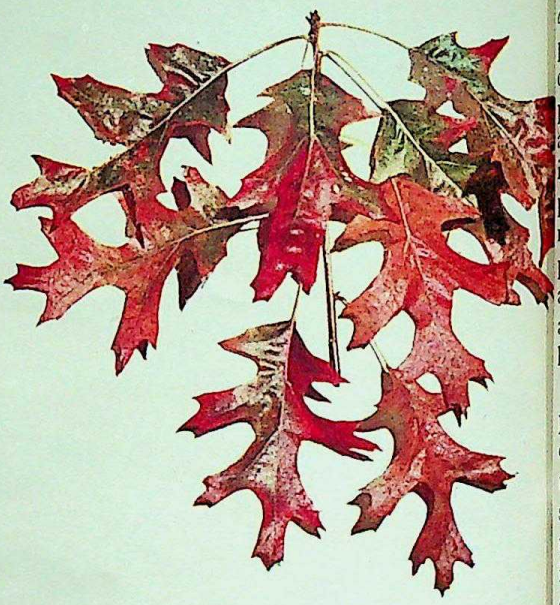


FIGURE 10 – Quercus coccinea.

FIGURE 11 – Platanus acerifolia, *showing acceleration of yellowing (on left) caused by treatment with coal-gas.*

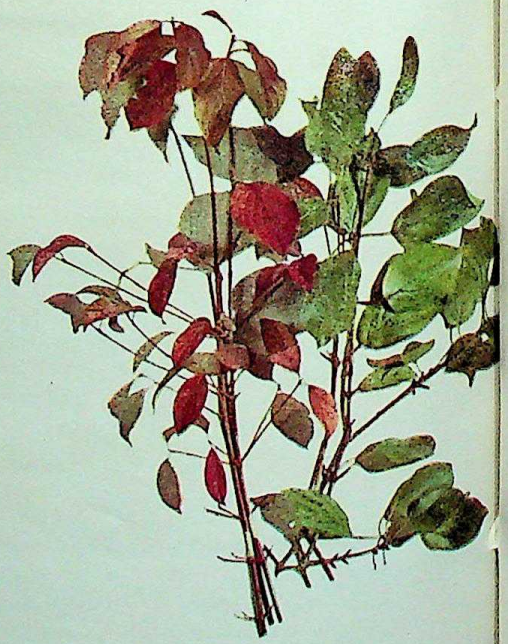


FIGURE 12 – Cornus sanguinea, *showing red colora*
produced by ringing the shoots on the left.

red pigments that are soluble in water and so are present throughout the aqueous cell liquids, e.g. the red colouring-matter of beetroot. These are *anthocyanins*; they are not universally present in plants, and even species which can make them do not always do so. When they occur, their presence is associated particularly with the appearance in the cells of large amounts of sugar. There is no pigment normally present in leaves which produces a brown colour. This is the result of post-mortem changes—oxidations akin to the browning produced when a cut apple or potato is exposed to air. Otherwise, the colours which appear in autumn are those due to combinations, or to a local predominance, of the normal pigments.

It has already been pointed out that, from the point of view of the plant functions, autumn colours are associated with the process of evacuation of valuable materials. Chemical analysis shows that this process is generally started by the transformation of starch (an insoluble food reserve) into sugars. This is the stage at which the red colours (anthocyanins) may first appear, for, as already noted, their formation is generally correlated with a high sugar content. The next stage is marked both by the removal of the last reserves of carbonaceous or sugary foods and at the same time by the mobilization and removal of the green pigments. The leaves then go yellow because the yellow pigments become predominant, not because new colours are formed, and this fact is well illustrated by the following figures for the pigments present in sycamore leaves during the process of yellowing:

Pigments present in yellowing sycamore leaves

Days	Colour of leaf	In per cent. of original amounts		
		Chlorophyll	Xanthophyll	Carotene
0	Green ..	100	100	100
3	Light green	59	89	100
5	Yellow ..	16	72	95
7	Brown ..	2	45	63

During yellowing, the final reserves of substances capable of yielding the sugars necessary for anthocyanin formation are now converted into sugar, so that here is a second—and also a last—opportunity for the leaf to become red. After this stage the leaf is finally depleted both of its food reserves and of the pigments necessary to manufacture more food. It quickly dies, and at the same time dries, turning brown.

While these colour changes follow a more or less uniform pattern they show considerable differences in intensity, which can be traced to differences in the internal or external conditions. The beautiful autumnal effects seen in our English woodlands would pale into insignificance if put alongside the flaming colours of many North American forests. The difference is, of course, partly due to the peculiarities of the trees; both maples (*cf.* figure 9, which is not, however, North American) and also oaks, like *Quercus coccinea* (which is often planted in Britain, figure 10) contribute to it, as well as some of the shrubs (*cf.* figure 4). But there are also differences due to the temperature conditions. The North American 'Indian summer,' when the colours are at their best, is usually markedly bright with frosty nights, conditions which favour the production of red pigments. In like manner, it can be noticed in Britain that a frosty autumn with bright days between the frosts almost always gives much better colours—in particular, reds—than one observes during a wet autumn, when dull yellows and dirty browns predominate. These differences are clearly due to environmental influences. The rapid appearance of dull yellows and browns in a wet autumn is like the similar effect produced when greenhouse plants are too frequently watered. This treatment removes various soluble substances from the leaves, especially potassium salts, which appear to be associated with the normal water-retaining capacity of a leaf. Their removal is associated with the early drying and death of the leaves, which may even precede the usual yellowing changes.

For the explanation of these other colour effects we have to look to the effects of temperature upon sugar accumulation, and hence upon the resultant anthocyanin formation. At low temperatures, near the freezing point, insoluble substances like starch are very rapidly converted into sugar, although the rate at which the sugars can leave the leaf is decreased by low temperatures. The resultant accumulation of the sugar leads to red pigment formation. A similar effect is obtained when potatoes are exposed to temperatures near the freezing point, for after this treatment they become sweet to the taste. Trees, moreover, show a similar effect in spring when the starch stored in the trunks is being converted to sugar. The sugar maple (*Acer saccharum*) gives, therefore, much larger yields of sugary sap after cold nights.

Any other treatment which leads to accumulation of sugar in the leaves is liable also to cause the production of red colours in autumn. Experimentally, sugar can often be made to accumulate by preventing its transport from a leaf or leafy shoot. One way of doing this is to 'ring' the shoot, that is, to scrape off all the soft outer tissues through which most of the sugar transport takes place. When this is done in autumn, sugar necessarily accumulates in the leaves and they turn red if suitable plants are used. Twigs of dogwood (*Cornus sanguinea*) treated in this way are shown in figure 12, along with untreated twigs of similar origin. Privet, especially the wild forms, and elder are also useful for this purpose, but plants which do not normally form red pigments are useless (e.g. the British oaks and beech).

It is sometimes possible to produce the same effect (if the twigs are not too brittle) by bending back a branch, so as to constrict the conducting tissues and prevent sugar transport. In North American sugar maples, sugar accumulation and red colour production can be increased by fastening branches with the tip vertically downwards, but this does not seem to be successful with our English sycamore (*A. pseudoplatanus*), which forms red pigments less easily.

The yellowing changes are also affected by external conditions. A leaf can be induced by suitable treatment to turn yellow at almost any time. The simplest way of accomplishing this is to keep it in darkness for some days, and if this is done with a series of leaves of different ages, it will be found that the old ones yellow first, while the young ones are comparatively resistant to the onset of yellowing changes. The same thing happens during the autumn colour changes. Young leaves, that is those nearest the stem apex, are generally the last to change colour, and this is shown in the leaves of the tulip-tree, *Liriodendron tulipifera*, illustrated in figure 1.

Simple experiments like cutting through a vein will usually retard the onset of yellowing in part of a leaf, merely because this treatment prevents the soluble substances which are formed from being removed. We learn thus that the veins in a leaf are the actual means of transport, although some movement may take place through the intervening tissues. The distribution of autumn colours is usually in accordance with this, for the yellowing changes are normally most rapid along the veins and often occur first in the basal leaflets, from which evacuation is most easy. Drying, and the resultant production of brown colours may appear first at the edge of the leaf and between the veins, though they do not do so in any of the examples figured here.

Yellowing is also more rapid if the leaves remain attached to some part of the plant that is using the materials transported away from the leaf. Thus leaves on an actively growing stem, or on one bearing developing fruits, will turn yellow more quickly than similar leaves detached and kept with their stalks in water.

Finally, the yellowing changes are also dependent upon other conditions as well as upon the presence or absence of light. One of the curious effects of external conditions can still be seen occasionally near street gas-lamps, though it is less obvious nowadays than it was in the days when old-fashioned jet-burners were employed. It was noticed at that time that the leaves turned yellow and died on trees near street lamps much more quickly than they did when growing some distance away from them. This was finally traced to the presence of unsaturated hydrocarbons like acetylene and ethylene, which were present in the coal gas. These substances markedly accelerate the changes which lead to yellowing. Thus of similar samples of leaves, those kept in air containing coal-gas (or acetylene or ethylene) will yellow more quickly, as is shown in figure 11. Ripening fruits like green bananas can also be made to yellow more quickly by this method. It is a curious fact that some fruits, apples for example, give off small quantities of compounds such as ethylene, so that the presence of one fruit may accelerate the yellowing or 'ripening' of another. This is one of the reasons why it is advantageous to wrap up stored apples in paper. The fact is interesting also because it shows that the ripening of a fruit, though proceeding far more slowly, is in many respects analogous to the yellowing of a leaf, so that the information we can obtain about one of these processes is very often capable of being applied to the other. Both are interesting as examples of that mysterious sequence of events we call senescence.

The *Opus maius* of Roger Bacon

A. C. CROMBIE

may be regarded as appendices
tion to science. This celebrated
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Aristotle in his *Posterior Analytics* and

to Aristotle, scientific investigation
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and the second deductive. The

1914; Roger Bacon,' *Proceedings of the British Academy*, 1928, 14, pp. 265 *et seq.*; J. E. Sandys, 'Roger Bacon in English Literature,' in *Roger Bacon Essays*; Lynn Thorndike, *A History of Magic and Experimental Science*, New York, 1923, vol. 2, pp. 679 et seq.

acon's life see J. H. Bridges, *The Life and Work of Roger Bacon*, London, 1914, and A. G. Little, *op. cit.*

[3] On Aristotle see W. D. Ross, *Aristotle*, 3rd ed., London, 1937, pp. 41–55; R. McKeon, 'Aristotle's Conception of the Development and the Nature of Scientific Method,' *Journal of the History of Ideas*, 1947, 8, pp. 3 et seq.

Any other treatment which leads to accumula-
tion of sugar in the leaves is liable also to cause the
production of red colours in aut
mentally, sugar can often be made
by preventing its transport from a
shoot. One way of doing this is
shoot, that is, to scrape off all
tissues through which most of the s
takes place. When this is done in
necessarily accumulates in the le
turn red if suitable plants are used.
wood (*Cornus sanguinea*) treated in
shown in figure 12, along with unt
similar origin. Privet, especially t
and elder are also useful for this
plants which do not normally form
are useless (e.g. the British oaks anc

It is sometimes possible to proc
effect (if the twigs are not too britt
back a branch, so as to constrict t
tissues and prevent sugar transpc
American sugar maples, sugar acc
red colour production can be incre
ing branches with the tip vertica
but this does not seem to be s
our English sycamore (*A. pseudopl*
forms red pigments less easily.

The yellowing changes are als
external conditions. A leaf can
suitable treatment to turn yellow
time. The simplest way of accompl
keep it in darkness for some days,
done with a series of leaves of di
will be found that the old ones yel
the young ones are comparatively
onset of yellowing changes. Th
happens during the autumn cc
Young leaves, that is those nearest
are generally the last to change col
shown in the leaves of the tulip-tr
tulipifera, illustrated in figure 1.

Simple experiments like cutting
will usually retard the onset of yello
a leaf, merely because this treatme
soluble substances which are form
removed. We learn thus that the
are the actual means of transport,
movement may take place throu
vening tissues. The distribution of a
is usually in accordance with this, for the yellow-
ing changes are normally most rapid along the

The *Opus maius* of Roger Bacon

A. C. CROMBIE

The *Opus maius*, and the *Opus minus* and *Opus tertium* which may be regarded as appendices to it, comprise the essential parts of Roger Bacon's contribution to science. This celebrated Somerset friar has always proved somewhat of an enigma to historians—whether of science or not—and little agreement has been reached in estimating how far he possessed the true spirit of science. Dr Crombie makes an important contribution to the discussion.

Since his death (probably in the year 1292) Roger Bacon's reputation has passed through various phases, each of which represents a different way in which he has caught the imagination of mankind. Almost from the beginning there has been a Roger Bacon of legend as well as of fact[1], and quite apart from his actual contributions to science he has been used by different ages as a symbol for their own beliefs and aspirations. For the 16th century, as for the 14th, Roger Bacon was a magician, who attempted to gain power over nature and mankind by tapping occult and dangerous forces, who had made a monstrous brazen head:

> 'That, by the inchaunting forces of the Devil,
> Shall tell out strange and uncoth Aphorismes,
> And girt faire *England* with a wall of brasse.'

For the 19th century he was again a symbol of the desire for power over nature, but then he was thought of as a 19th century scientist born before his time, impatiently trying to break through the web of metaphysical pseudo-problems which entangled his contemporaries—in fact as an early positivist. More recently, historical scholarship has made it possible to deny that

> 'The fame of *Bacon*, bruted through the world,
> Shall end and perish with this deepe disgrace,'

but has also created a further legend: that he deserves no reputation at all beyond that of a querulous nuisance.

The whole truth about Roger Bacon's position in the history of science is something much more complex than any of these legends, and can be understood only by trying to discover the problems with which he was faced and the particular historical circumstances in which he found himself. An intellectual revolution was brought about in Western Christendom by the translation during the 12th and early 13th centuries of the major works of Greek and Arab science and philosophy, and when, in 1266–7, Bacon wrote the *Opus maius* in response to Pope Clement IV's request, his first problem concerned the attitude to be taken to this new knowledge.[2] Following the lead of such men as Robert Grosseteste in Oxford and Albertus Magnus in Paris and Cologne, he tried to show that natural science, far from being a danger to Christendom, was a source of both wisdom and power. The *Opus maius* is in effect a programme of educational reform based on three principal studies—of languages because these were the key to earlier knowledge and to the Bible, in which it was held that all wisdom was contained, at least by implication; of mathematics; and of experimental science. The last two doors to knowledge were the means of investigating nature directly, and it was through his grasp of the possibilities of mathematics as a means of explanation and practical use, and of the role of induction and experimental verification in scientific research, that Roger Bacon made his most important contribution to science. He put forward his ideas on these subjects as an extension of those already advanced by Aristotle in his *Posterior Analytics* and *Physics*.[3]

According to Aristotle, scientific investigation and explanation constituted a twofold process, the first inductive and the second deductive. The

[1] For an account of attitudes to and historical research on Roger Bacon see A. G. Little, 'On Roger Bacon's Life and Works,' in *Roger Bacon Essays*, ed. A. G. Little, Oxford, 1914; 'Roger Bacon,' *Proceedings of the British Academy*, 1928, 14, pp. 265 *et seq.*; J. E. Sandys, 'Roger Bacon in English Literature,' in *Roger Bacon Essays*; Lynn Thorndike, *A History of Magic and Experimental Science*, New York, 1923, vol. 2, pp. 679 et seq.

[2] For Roger Bacon's life see J. H. Bridges, *The Life and Work of Roger Bacon*, London, 1914, and A. G. Little, *op. cit.*

[3] On Aristotle see W. D. Ross, *Aristotle*, 3rd ed., London, 1937, pp. 41–55; R. McKeon, 'Aristotle's Conception of the Development and the Nature of Scientific Method,' *Journal of the History of Ideas*, 1947, 8, pp. 3 et seq.

investigator must begin with what is prior in the order of knowing, that is with facts observed through the senses, and ascend by induction to generalizations or universal forms or causes which are most remote from sensory experience. These universal forms are prior in the order of nature, and the second process in science is to descend again by deduction from them to the observed facts, which are thus explained as following from more general principles which are their cause. The most exact sciences according to Aristotle, and the only ones really deserving the name of science, were those in which the effects could be shown to follow necessarily from their causes as conclusions from premises, and the model of such sciences was mathematics. Where mathematics could be used in the natural sciences the deductions were also exact and necessary, as for instance in astronomy, where the movements of the heavenly bodies could be expressed in geometrical terms, and in optics, where the laws of light were geometrical. These ideas of Aristotle on induction and mathematical demonstration were taught in Oxford by Robert Grosseteste,[1] who said that it was impossible to investigate nature without observation and experiment and to understand it without geometry, and Grosseteste was hailed by Roger Bacon as his master.

Mathematics for Bacon was the 'gateway and key to all other sciences,'[2] the only science capable of giving 'demonstrations of the most convincing kind through a necessary cause.'[3] This he had every reason to believe, because the most mature part of the science that the Latin Christians had learnt from the Greeks and Arabs was mathematical, and in the astronomical system of Ptolemy, the work on optics of Euclid, Ptolemy, and Alhazen, and various works on mechanics based on Euclid and Archimedes, they had examples of exact, demonstrative science. These subjects had excited the greatest interest among Western scientists.

The Ptolemaic system was discussed by nearly every natural philosopher of the 13th century, and it was modified and its range of explanation extended as a result of observations and measurements of the positions of stars and planets with the astrolabe, quadrant, cross-staff, and other astronomical instruments. In optics, the Greek and Arabic writings contained demonstrations of the principles that light travels in straight lines in one medium, and that with reflected light the angles of incidence and reflection are equal; of the phenomenon of refraction (though not the exact mathematical law, which was in fact not formulated till the 17th century); and of many of the properties of plane, convex, and concave mirrors and of lenses. Beginning with this knowledge, Grosseteste tried to improve the theory of refraction and to explain the rainbow, and the Polish physicist Witelo made refraction tables for air, water, and glass. In mechanics, the Dominican mathematician Jordanus Nemorarius and his school demonstrated the law of the lever, and discovered how to determine the component of gravity acting on a body on an inclined plane, an identical proof of which was later given by Stevinus.

This work of his predecessors and contemporaries in mathematical physics Bacon used in Parts IV (Mathematics) and V (Optical Science) of the *Opus maius*, to illustrate the principle that facts observed in the natural sciences are made intelligible, and usable, when they are shown to be the result of mathematical laws; and he tried to extend the application of mathematics to a variety of other problems. He analysed the astronomical grounds for the error in the Julian Calendar, which by the 13th century had become so inaccurate that, as he said, 'any rustic' who looked at the sky could see 'that the new moon occurs as a matter of fact 3 or 4 days before it is marked on the calendar,'[4] and he arrived at a more accurate figure for this error than any previously reached. He tried to calculate the size of the universe, the distances between the planetary spheres, and the dimensions of the sun and moon; to plot the positions of towns and countries on a map; to arrive at the law of freely falling bodies; and to discover the limits of probability in predicting events by astrology, where he held that the planets may influence the human body but not the will, which was free, and that God's omnipotence introduced an element of uncertainty into all judgments about the future.

The chief part of his discussion, however, is taken up with the laws of geometrical optics, and

[1] Mainly in his commentary on the *Posterior Analytics* and his opuscula on optics and astronomy. For the latter see L. Baur, 'Die Philosophischen Werke des Robert Grosseteste, Bischofs von Lincoln,' in *Beiträge zur Geschichte der Philosophie des Mittelalters*, 1912, 9; and 'Die Philosophie des Robert Grosseteste, Bischofs von Lincoln,' *Beiträge* . . ., 1917, 18, Hft. 4–6.

[2] *Opus maius*, IV, distinctio i, cap. 1.

[3] *Opus maius*, IV, distinction i, Ch. 3; R. B. Burke, *The Opus maius of Roger Bacon*, Philadelphia, 1928, p. 124. All quotations are from this translation, to which page references are given.

[4] *Opus maius*, IV; Burke, p. 296.

in these he had particular reasons for interest. First, he held that all natural operations in the region below the moon were brought about by the propagation of rays of force, or, as he called it, 'virtue' or 'species,' a theory which in fact went back at least to Lucretius and was very popular among Arab writers.[1] Rays of 'species' or force from the moon, he held, drew up from the sea-floor vapour which pushed up the high tide. Rays from the sun and planets affected the climates of different localities, and rays of astrological influence, acting according to the configuration of the heavens, upset human physiology and affected men's disposition to certain actions; for example, the dreadful comet of July 1264, which was shown to have been generated by Mars, produced an increase of jaundice, leading to bad temper, and the result was the wars and disturbances in England, Spain, and Italy at that time and afterwards! Rays shone forth also from the human soul; Bacon himself had seen a physician blinded by 'species' from the eyes of a diseased patient he was trying to cure; and Antichrist, against whose coming Bacon wished to prepare Christendom, would certainly harm his victims with malignant glances. The type of such a propagation of force or 'species' was light, and with that particular medieval facility for seeing everything implied in everything else, Bacon learnt from St Augustine to see in light the analogy of divine grace and the illumination of the human intellect by divine truth. The study of light was therefore in a special way the key to nature and to truth.

For his basic knowledge of optics Bacon made use of the earlier Greek, Arabic, and Latin Christian writings, and what he added to these was a critical attention to particular problems, with an emphasis on method and on practical applications. He gave a better description of the anatomy of the vertebrate eye and the optic nerves than any previous writer, and recommended that those who wished to study the subject should dissect the eyes of cows or pigs. He pointed out that the sun's rays reaching the earth may be treated as parallel instead of radiating out from a point, thus making possible a better explanation of burning lenses and parabolic mirrors; he discussed in detail the conditions necessary for vision, and working on the theory that the apparent size of an object depends on the angle it subtends at the eye, tried to improve vision by means of lenses. His scientific imagination played freely with the possibilities of indefinitely magnifying small objects and bringing distant objects near, by suitable arrangements of mirrors or lenses. He held that Julius Caesar had erected mirrors in Gaul with which he saw what was going on in England, and that lenses might be used to make the sun and the moon descend and appear above the heads of enemies; the ignorant mob, he said, could not endure it.[2] Spectacles actually came into use a little before the year 1300[3], but the compound microscope and telescope had to wait another three centuries for Galileo and his optic glass.

The mathematical method, as seen in optics, was able to render nature intelligible by making it possible to deduce observed effects from their causes, but neither Aristotle nor any other Greek or Arab writer had given any precise indications of how first to arrive at these causes. This Bacon tried to provide for in his Experimental Science,[4] which forms Part VI of the *Opus maius*, and this, with the previous work of Grosseteste, is possibly the most important contribution to the experimental method between Aristotle or Archimedes and Francis Bacon and Galileo. What Roger Bacon called *Experientia* was both a method and a body of knowledge gained by this method, and its prerogatives were (1) to confirm the conclusions of mathematical reasoning, (2) to add to deductive science knowledge at which it could not itself arrive and (3) to discover departments of knowledge still unborn. As a method of induction, in which he showed how the investigator passes from observed effects to the discovery of the cause and isolates the true cause by eliminating theories contradicted by facts, his procedure is best seen in his attempt to discover the cause of the rainbow. He began by collecting phenomena similar to the rainbow—colours in crystals, in dew on the grass, in spray from mill wheels or oars, or as seen when the sun was looked at through a

[1] On this theory see C. Baeumker, 'Witelo, ein Philosoph und Naturforscher des XIII. Jahrhunderts,' *Beiträge . . .*, 1908, 3, Hft. 2; L. Baur, 'Das Licht in der Naturphilosophie des Robert Grosseteste,' in *Festschrift Georg von Hertling*, Freiburg.-i.-B., 1913; 'Der Einfluss des Robert Grosseteste auf die wissenschaftliche Richtung des Roger Bacon,' in *Roger Bacon Essays*, ed. A. G. Little, Oxford, 1914; L Thorndike, *op. cit.*, vol. 2, pp. 642 et seq.

[2] Donne suggested a similar use for Galileo's telescope in his polemical work, *Ignatius his Conclave*.

[3] See C. Singer, 'Steps leading to the invention of the First Optical Apparatus,' in *Studies in the History and Method of Science*, ed. C. Singer, Oxford, 1921, vol. 2; G. Sarton, *Introduction to the History of Science*, Baltimore, 1931, 2, pp. 1024 et seq.

[4] See on this, R. Carton, 'L'expérience physique chez Roger Bacon,' *Etudes de Philosophie Médiévale*, Paris, 1924, No. 2.

hat or piece of cloth or through the eyelashes. He then examined the rainbow itself, noting that it appeared always in cloud or mist, and by a combination of observation, astronomical theory, and measurements with the astrolabe was able to show that the bow is always opposite the sun; that the centre of the bow, the observer's eye, and the sun are always in a straight line; and that there is a definite connection between the altitudes of the bow and of the sun. To explain these facts he then advanced the theory put forward in Aristotle's *Meteorologica* (III, 2–6), that the rainbow forms the base of a cone of which the apex is at the sun and the axis passes from the sun through the observer's eye to the centre of the bow. The base of the cone would become elevated and depressed, thus producing a larger or smaller rainbow, according to the altitude of the sun, and if it could be sufficiently elevated the whole circle would appear above the horizon, as with rainbows in sprays. This theory he used to explain the height of the bow at different latitudes and different times of year. It would imply among other things that each observer would see a different bow, and this he confirmed by the observation that when he moved towards, away from, or parallel to the rainbow it moved with him relative to trees and houses; a thousand men in a row, he asserted, would see a thousand rainbows, and the shadow of each would bisect the arc of his bow. The colours and form of the rainbow, he held, therefore bore to the observer a relation unlike those of fixed objects such as crystals. About the colours, Bacon's discussion was as unconvincing as that of everyone else till Newton; the form he explained as due to reflection from spherical water drops in the cloud, the rainbow of any particular observer appearing only in the drops from which the reflected rays went to his own eyes. This theory he extended to try to explain halos and mock suns. It was not in fact correct, and the correct explanation was given a little later by a younger contemporary of Bacon's, Theodoric of Freiberg (d. 1311) (following Al-Farisi),[1] and again more fully by Descartes in his *Dioptrique*.

Bacon's ideas on the mathematical and experimental methods had an immediate and lasting influence on his successors.[2] He seems to have inspired the study of optics and physics in Oxford, and of astronomy in Paris, at the end of the 13th century. He was famous throughout the later middle ages as an alchemist, and his medical writings were collected in the 14th century and were still being used by physicians in the 17th. His idea that there was no great width of ocean between Spain and India indirectly influenced Columbus; his work on the correction of the calendar seems to have led to the suggestion that Copernicus should undertake the same task; and the section of the *Opus maius* on Optics was continuously copied, was printed as late as 1614, and must have been known to Kepler and Galileo. So his prophetic imagination has at least some strands of connection with real history.

But later ages gradually forgot the primary purpose of Roger Bacon's suggested reforms and what they meant to himself, and created the legend of him as the prophet of pure utilitarianism. So to conceive of him would be to contradict everything we know about his age and entirely to miss the point of the *Opus maius*. When

> 'science held her seate
> Between the circled arches of (his) browes,'

it was not simply for acting 'strange and uncoth' miracles; and in the last part of the *Opus maius*, which is concerned with what he called Moral Science, he gathered up the other parts into their ultimate function, namely to protect Christendom and to assist the Church in her work of evangelizing mankind by leading the mind through scientific truth to the contemplation of the Creator already revealed in theology, a contemplation in which all truth was one. This was the real purpose of power and wisdom and the ultimate utility.

[1] E. Krebs, 'Meister Dietrich (Theodoricus teutonicus de Vriberg), sein Leben, seine Werke, seine Wissenschaft,' *Beiträge* . . . , 1905, 5, Hft. 5–6; J. Würschmidt, 'Dietrich von Freiberg über den Regenbogen und die durch Strahlen erzeugten Eindrücke,' *Beiträge* . . ., 1914, 12, Hft. 5–6; cf. P. Duhem, *Etudes sur Léonard de Vinci*, Paris, 1906, vol. 1, pp. 171 et seq.

[2] On Roger Bacon's influence see J. H. Bridges, *op. cit.*; A. G. Little in *Roger Bacon Essays*, pp. 24 et seq.; P. Duhem, *Le Système du Monde*, vol. 3, pp. 446 et seq., 511 et seq.; D. E. Sharpe, *op. cit.*, pp. 117–20; L. Thorndike, *op. cit.*, vol. 2, pp. 616 et seq.

Imitating the clouds

M. W. CHIPLONKAR

A good method of learning is to imitate, and the history of science abounds in pioneer experiments deliberately arranged to imitate Nature. An attempt has been made in this article to show how imitation has helped us to get an insight into the various physical processes going on in the atmosphere, which often produce most beautiful and arresting clouds.

To the scientific mind clouds present an almost unlimited field of inquiry, and it is an absorbing problem to try to understand and imitate their shapes. It is clear that to attempt to solve the problem purely mathematically is an utterly hopeless task, and one has to fall back on some sort of experimental method. Here too the challenge of only the simpler and not the complicated problems has to be taken up if one wishes to achieve anything like success. The more regular and uniform patterns are obviously the most likely to be due to simple physical conditions existing at the time in the atmospheric layers in which they are produced. In fact, it is these simple regular patterns of natural clouds that have been well imitated in the laboratory in recent times.

At first, Helmholtz and Lord Kelvin tried to explain theoretically the processes underlying the formation of such cloud patterns in the sky, taking for their basis the relative movements of the neighbouring air layers; they were, however, not successful. H. Benard, and later P. Idrac and T. Terada, suggested from their laboratory experiments that the patterns might be due to the same process as that which gives rise to the convection cells (now known as Benard cells, figure 1) in a shallow unstable layer of a fluid. It is also reported that this kind of regular organized movement was observed much earlier by Weber, in very thin films of liquid mixtures on a microscope slide, and also by James Thomson in deeper layers of soapy solutions left undisturbed in an open tub. The experimental work of later investigators on instability layers of fluids, with or without a superposed general shear, has not only supported their suggestion but has further elucidated many other points of detail demanded by the theory developed first by Lord Rayleigh and later modified by Harold Jeffreys.

In the course of his studies on clouds, natural and artificial, the author was fortunate enough to secure a number of typical photographs of natural cloud patterns as they developed and dwindled away. An attempt is made in this article to present, out of that collection, a few typical natural cloud patterns side by side with their corresponding laboratory imitations,[1] and to discuss each briefly in the light of the above theory.

It is not very difficult to produce these cloud patterns in a laboratory. The photographs reproduced here were, however, obtained by employing specially constructed apparatus. A uniformly heated metal plate formed the bottom of a shallow chamber, and a long thick glass plate which could be moved in the direction of its length served as its top. The thickness of the air layer enclosed between the two plates (i.e. the height of the chamber) could be varied from a few millimetres to a few centimetres, by using accurate distance pieces. Heating at the bottom (or cooling at the top, or both) produced instability in the layer, and steadily moving the glass plate produced a uniform shearing motion in it. Tobacco smoke was introduced into it through a side tube to make visible the patterns formed in the air layer, which were then photographed from above under various known conditions.

For the purpose of this discussion the patterns are divided into the following three types:

I. Those showing irregular polygonal cells.
II. Those showing long rolls or waves with or without polygonal cells.
III. Those showing polygonal cells arranged in rows.

I. IRREGULAR POLYGONAL CELLS

Figure 2(*a*) is a photograph of an overhead strato-cumulus cloud taken at 11 a.m. on 10th April, 1939. There was no movement of the cloud as a whole in any direction, but the sheet of uniform cloud originally formed as a thin layer

[1] The author is greatly indebted to Mr K. Chandra for his laboratory imitations of cloud patterns reproduced in this article.

was seen to break up into numerous irregularly set polygonal cells (shown separately in the trace in figure 2(*b*)), and at the same time to grow thicker. The internal movements in this cloud did not produce any great changes in the pattern except the strengthening or weakening of some of the lines, and foci of descent. The cloud once formed was quite stable, and actually remained unchanged for more than an hour. An imitation pattern of the above is shown in figure 2(*c*), which is a photograph of an unstable layer of air mixed with smoke to make the movement visible. No bodily movement existed in this experimental layer either, but the dark lines and centres were seen to appear and disappear slowly. The resemblance between figure 2(*a*) and figure 2(*c*) is remarkable.

Figure 3(*a*) is a photograph of an overhead alto-cumulus cloud taken on a fairly clear day in October 1940. In this, the polygonal cells are much smaller in size and are more clearly defined. Here also very little, if any, movement of the cloud as a whole existed, but the cloud itself soon disappeared. A few of the polygonal cells are shown separately in figure 3(*b*), by tracing their boundaries. Figure 3(*c*) shows the corresponding type of cellular structure observed experimentally in a shallow layer (7 mm depth) with a large difference of temperature (130° C) between the top and the bottom of the layer. Here also the likeness between the natural and the artificial patterns is striking.

The movement of fluid in such a convection cell, the normal Benard cell (see figure 1), is that of a vertical ascent in the centre, a flow outwards from the centre in the uppermost layer, a vertical descent all along the periphery, and finally a flow inwards toward the centre in the lowest layer of the cell. In the sky, the white cloud material which may exist already, or which may be formed by fresh condensation above the ascending currents, is collected together at such places as C, C, while at A is formed the dark (blue sky) centre, and at places such as B, B is formed the dark (blue sky) boundary of the cells. When the supply of cloud material is abundant, the portions at C, C join up and the dark centre is not apparent. A circulation in the reverse direction is also possible, and is in fact often noticed in nature; the ascending current is along the periphery and the descending one at the centre of the cell. Such a process will obviously produce a pattern complementary to that of the normal Benard cell, i.e. a network of filaments of the white cloud material with empty circular blue patches of sky in the centre.

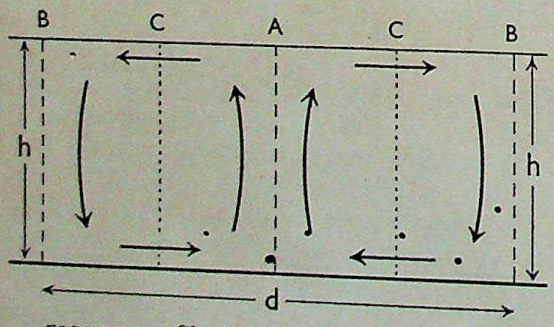

FIGURE 1 – *Circulation in a normal Benard cell.*

A very simple but interesting point may be raised here regarding the two motions. Are they not one and the same thing, except for a change of sign, the normal type of motion being as shown in figure 1 and the reverse motion as that shown when the same diagram is inverted or viewed upside down? Mathematically, the two motions represent the two solutions to the same problem of an unstable layer of fluid, and are identical except for a change of sign. Both solutions must be equally applicable, but in actual practice when working with a liquid it is found that the liquid always rises in the centre of the cell (normal type) whether we heat it at the bottom or cool it at the top; with air it always descends in the centre (reverse type). It has been suggested, after careful investigation, that the real explanation of this difference in motion is to be found in distinguishing the initial type of motion from the final steady viscous motion. The significant point to note here is that both types of motion actually occur in the atmosphere, and produce two distinct varieties of cloud patterns, depending on the prevalent conditions of temperature-lapse rate, humidity, etc., in the air layer. Figure 4(*a*), and its tracing in figure 4(*b*), provide an example of such a reticular pattern in nature, and figure 4(*c*) is its imitation in the laboratory. It presents the queer appearance of a sheet of white paper punched irregularly with circular holes. In this connection it may be pointed out that in the atmosphere, as it is actually constituted, more air goes up by chimney action than comes down; and it is this property of the atmosphere that, perhaps, favours the normal Benard cell or the chimney circulation more than the reverse one.

II. LONG ROLLS AND WAVES WITH OR WITHOUT POLYGONAL CELLS

Coming to the second group of patterns we see

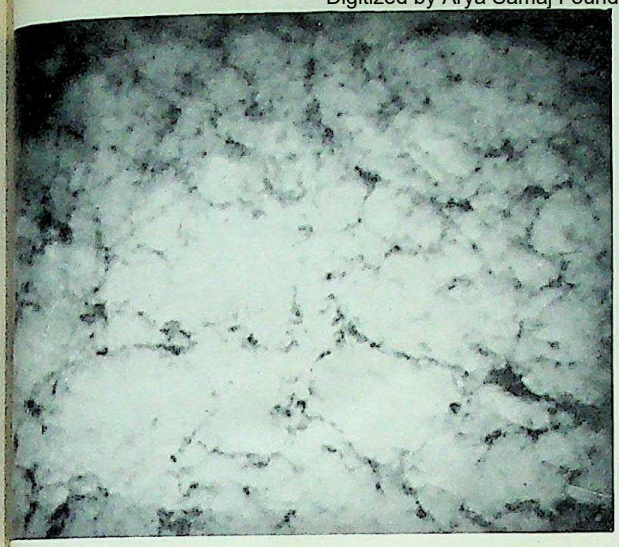

FIGURE 2(*a*)

FIGURE 3(*a*)

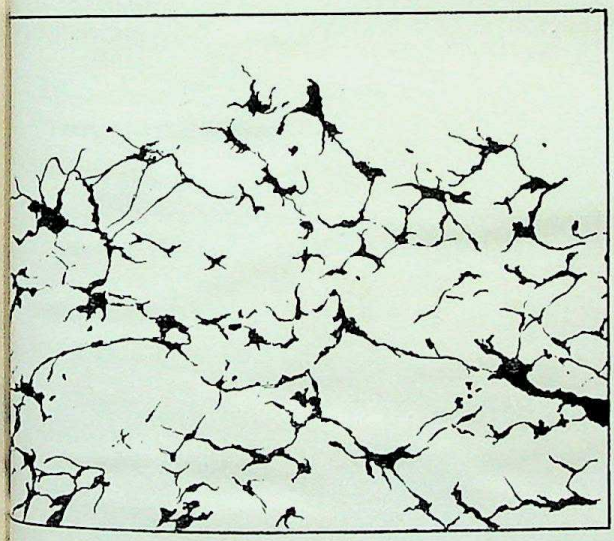

FIGURE 2(*b*)

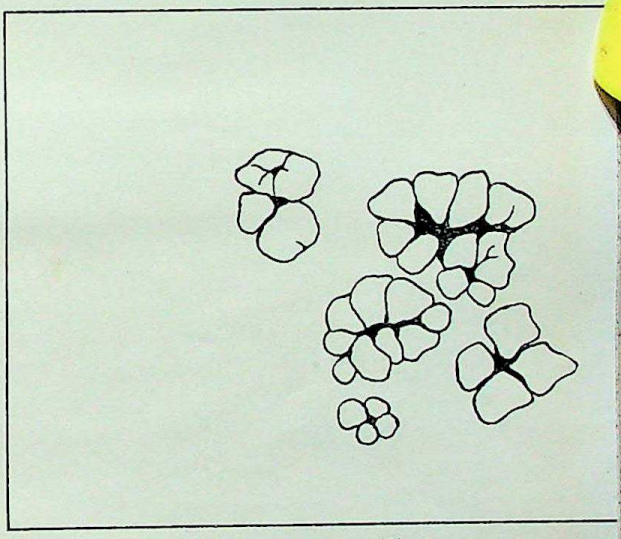

FIGURE 3(*b*)

FIGURE 2(*c*)

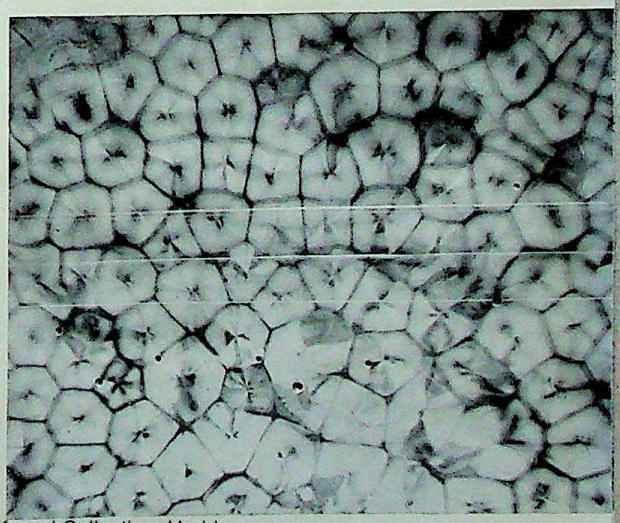

FIGURE 3(*c*)

FIGURE 4(*a*)

FIGURE 5(*a*)

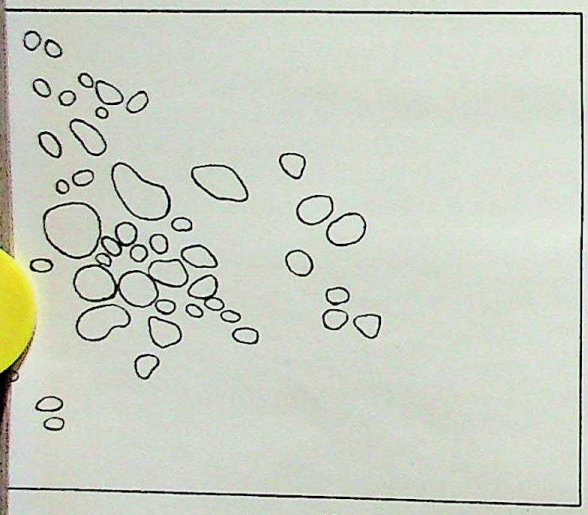

FIGURE 4(*b*)

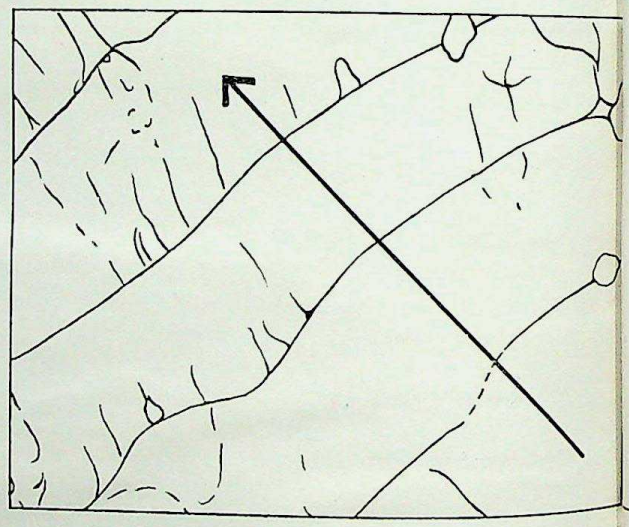

FIGURE 5(*b*)

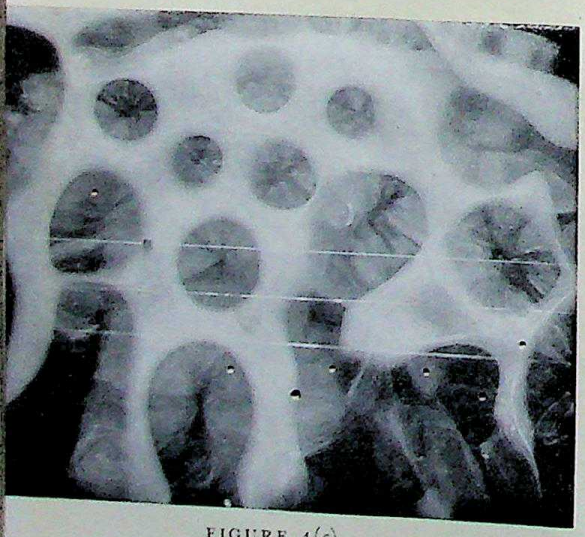

FIGURE 4(*c*)

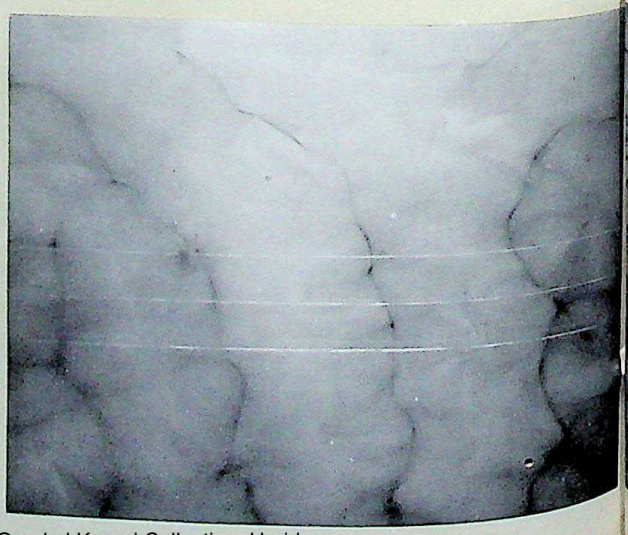

FIGURE 5(*c*)

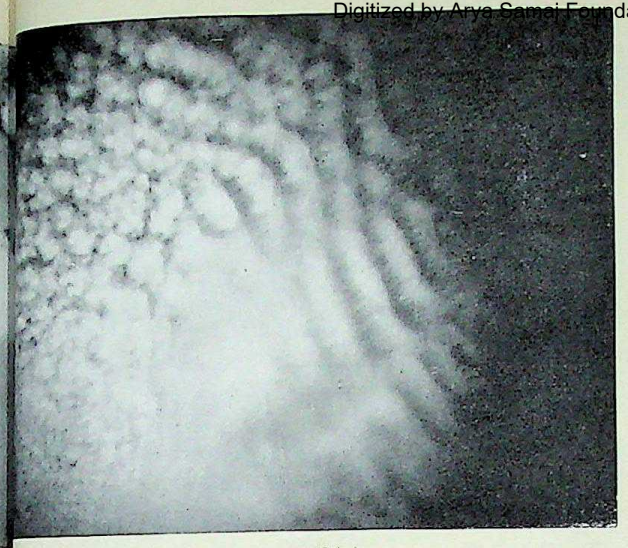

FIGURE 6(*a*)

FIGURE 7(*a*)

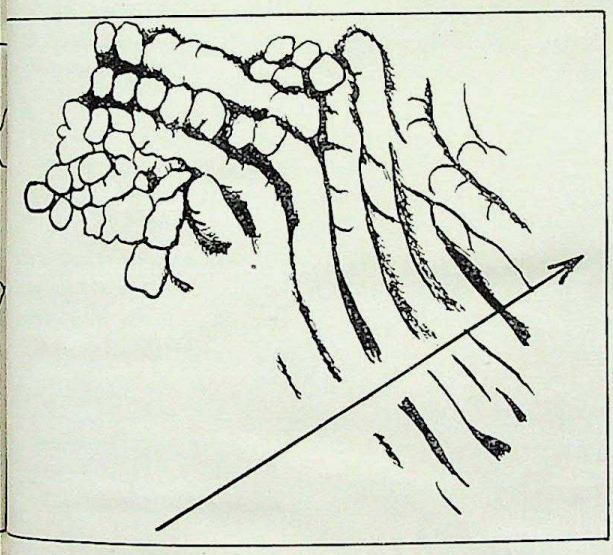

FIGURE 6(*b*)

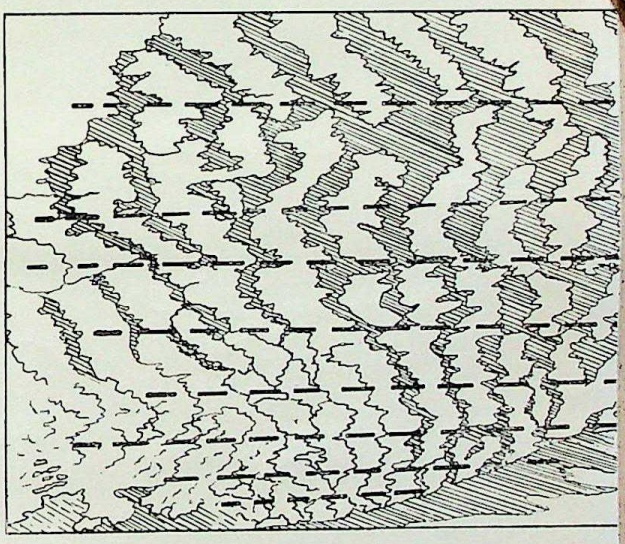

FIGURE 7(*b*)

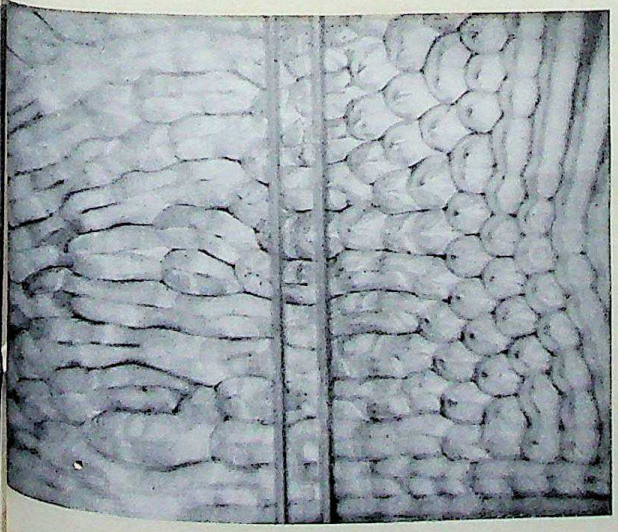

FIGURE 6(*c*)

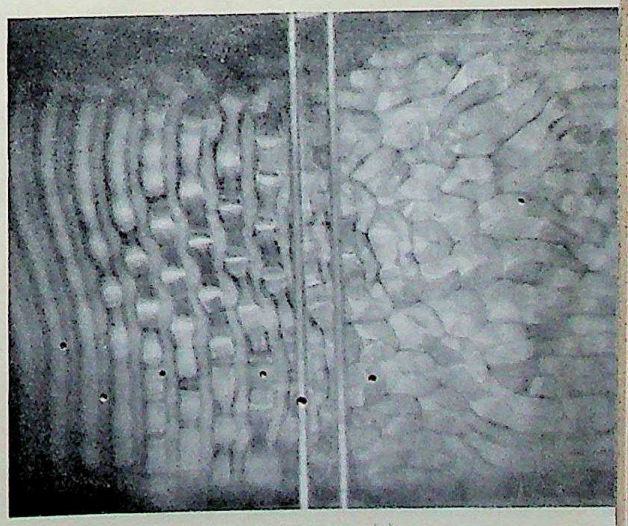

FIGURE 7(*c*)

Figure 7 (c) is reproduced by permission of the Royal Society.

FIGURE 8(*a*)

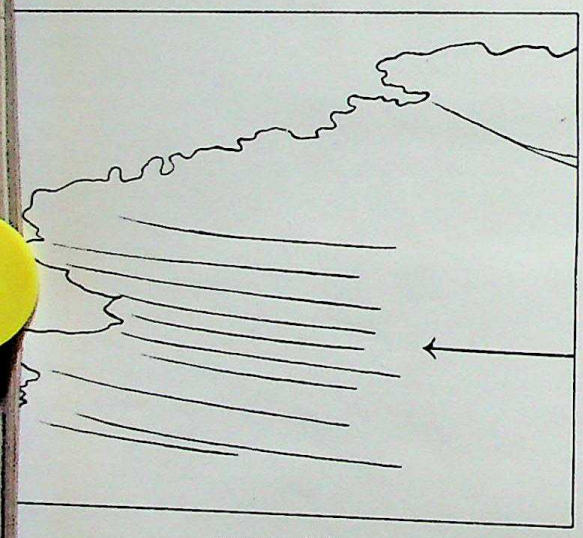

FIGURE 8(*b*)

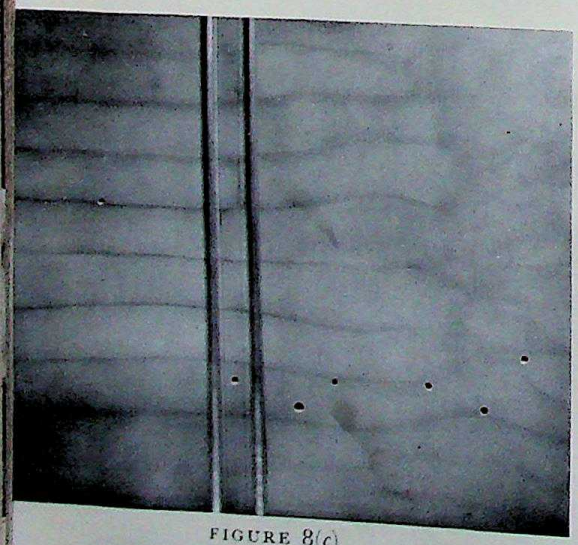

FIGURE 8(*c*)

that it includes two distinct types of roll structure: (1) transverse wavy rolls, and (2) longitudinal straight rolls.

1. *Transverse Rolls*

Figure 5(*a*) is a photograph of a very low alto-cumulus cloud with thick rolls taken on 12th April, 1939, with the camera pointing to the zenith. The cloud bank was observed to move as a whole in the direction shown by the arrow in the tracing in figure 5(*b*), with the rolls lying at right angles to it. The front sides of the rolls are very sharply defined, and each roll shows in itself a less defined structure of polygonal or round cells. The resemblance to the laboratory pattern, figure 5(*c*), which was developed in a 12 mm layer of air, with a temperature difference of about 95° C between the top and the bottom, and a small shear movement from the left to the right, is remarkably perfect. An extremely beautiful photograph of a wavy transverse pattern of an alto-cumulus cloud is shown in figure 6(*a*). In almost every cloud of this kind any small obstacle, or a sudden discontinuity in the physical conditions of the atmospheric layer, causes a break in the pattern, and it is continued from roll to roll in the direction of the shear. It will be noticed in the tracing, figure 6(*b*), that the various points of break in the different rolls lie on straight lines parallel to the direction of shear. This may also be regarded as a tendency to change over to a cross pattern, or to longitudinal rolls in the same sheet of cloud, as described later.

An interesting example of transverse rolls and polygonal cells in the same sheet of alto-cumulus cloud is shown in figure 7(*a*). This is one of a series of photographs taken on the morning of 19th July, 1939, with the camera almost facing the zenith. The sequence of movements showed that the cloud material of the freshly formed cellular pattern was gradually being moulded into the transverse rolls, owing to a small shearing motion at the cloud level. The direction of motion in the cloud marked by the lines in figure 7(*b*) is more or less normal to the length of the rolls produced. A very similar laboratory pattern was obtained under similar conditions, viz. the superposition of a small amount of shear on an already existing polygonal structure (see figure 7(*c*)). Actually the depth of layer was 8 mm, the difference of temperature between the top and the bottom was 90° C, and the shear was equal to 1·7 cm/sec approximately.

2. *Longitudinal Rolls*

The only convincing photograph of straight longitudinal roll cloud that the author could get is reproduced in figure 8(*a*). It is one of a series of photographs of the spread-out portion of the large anvil of a cumulo-nimbus cloud. It was taken late in the evening of 30th March, 1939. The rolls marked by the flow lines in the trace in figure 8(*b*) were actually seen to develop when the cloud was overhead, but at that time the lower scuds did not continuously allow a complete view of these rolls. The series of photographs could therefore be taken only after about 40 minutes, when the low clouds moved away. The whole anvil in the meantime had moved sideways, and presented a more or less profile view. When overhead (and to a less degree in the position shown in figure 8(*a*)) the rolls had a very close resemblance to the pattern in figure 8 (*c*), obtained in the laboratory while working with a layer of 16 mm depth, a small difference of temperature (about 30° C), and a large amount of shear (about 10 cm/sec).

It is occasionally observed that such rolls have wavy boundaries and are also bent at the ends (see figures 9(*a*) and 9(*b*)). They are mostly due to the original high shear falling at a later stage below a certain value, while the convection caused by the thermal instability still retains its original strength. The corresponding laboratory pattern shown in figure 9(*c*) was obtained while working with a layer of 16 mm depth, a large difference of temperature, and a comparatively small amount of shear, varying from 5 to 8 cm/sec.

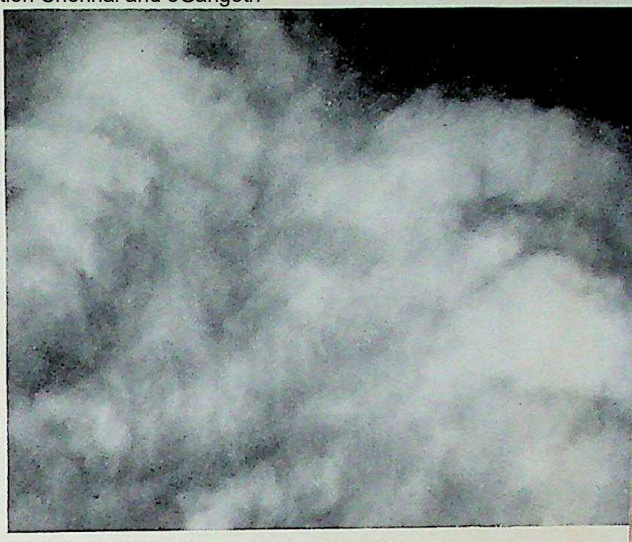

FIGURE 9(*a*)

FIGURE 9(*b*)

III. POLYGONAL CELLS ARRANGED IN ROWS

In this group all the cloudlets are arranged in two sets of parallel rows, and the shape of each cloudlet is determined by the angle between the rows. They can thus be rectangular or parallelogrammic.

An excellent example of such a pattern with rectangular cloudlets is shown in figure 10(*a*), and its tracing in figure 10(*b*). This pattern of alto-cumulus was photographed on 18th July, 1939, with the camera facing west at an angle of 50° above the horizon. The cloud was gradually evaporating, as is well seen in the series of pictures of this cloud. The pattern has been shown to be produced in the laboratory when an intermediate amount of shear is superposed on the thermal instability. Such conditions, being very critical, are somewhat difficult to attain. The cloudlets then arrange themselves either parallel and perpendicular to the direction of shear, or

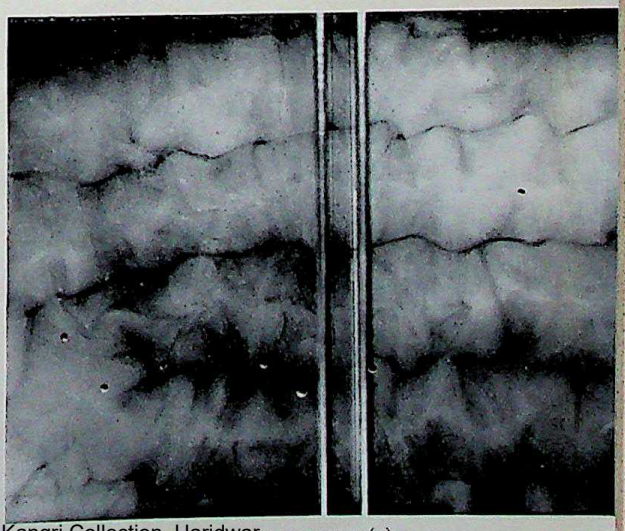

FIGURE 9(*c*)

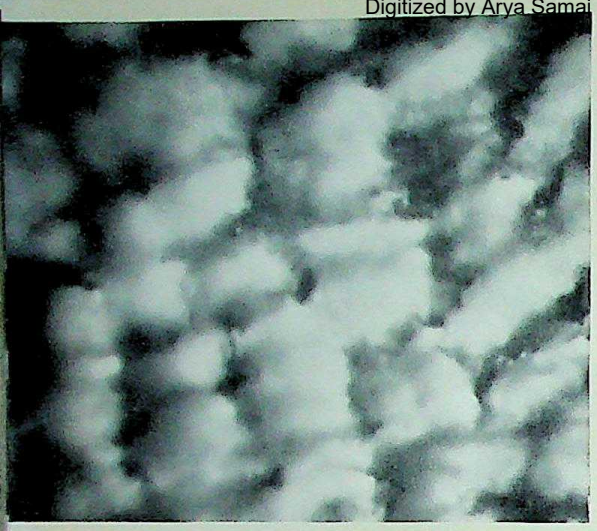

FIGURE 10(*a*)

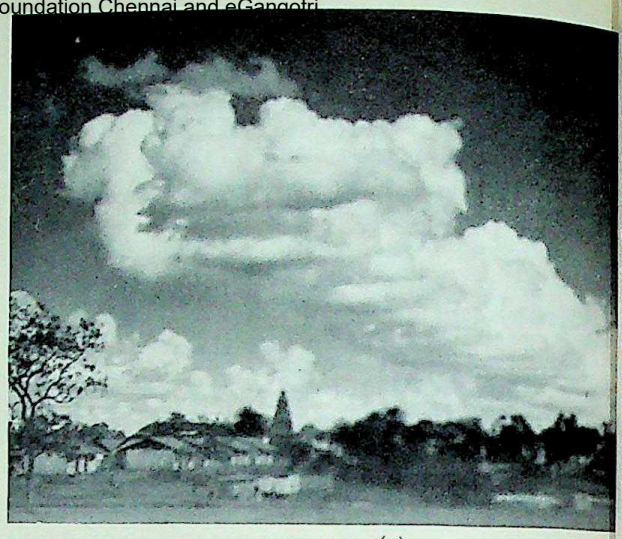

FIGURE 11(*a*)

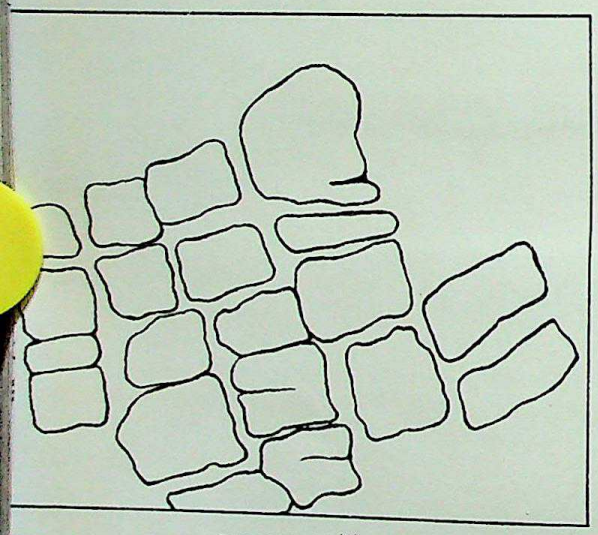

FIGURE 10(*b*)

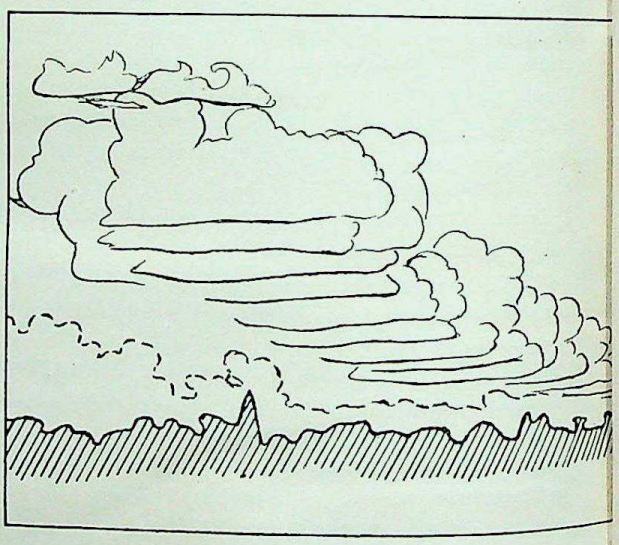

FIGURE 11(*b*)

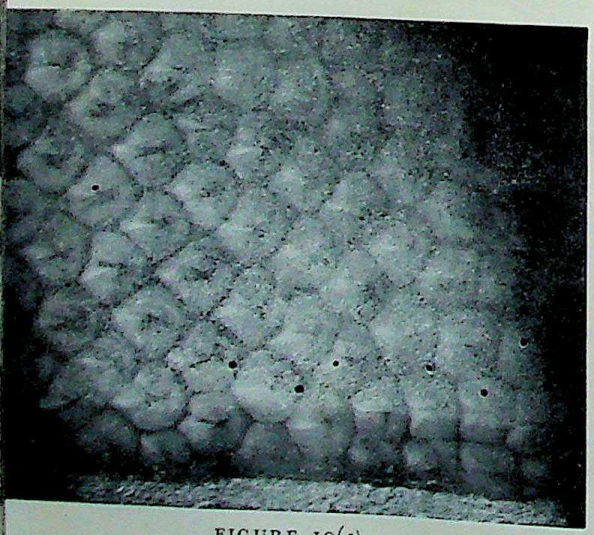

FIGURE 10(*c*)

at an angle of 45° to it. The laboratory imitation, which compares very well with this, is shown in figure 10(*c*), which is reproduced here from Sir Gilbert Walker's article in *Science Progress* (1935).

The cellular pattern associated with larger cumulus clouds has been found to be of great practical utility in modern times, and has attracted the attention of the aviator. A typical example of such a pattern is shown in figure 11(*a*) and its tracing in figure 11(*b*). Because of the perspective appearance it is sometimes called an echelon cloud. To the pilots of glider planes it is known as 'the cloud street.' Advantage is taken of the ascending currents of air under each cumulus to gain height, and the glider goes hopping from one cloud to another, i.e. from one centre of the convection cells to another.

What is a glass?

G. O. JONES and F. E. SIMON

From the standpoint of formal thermodynamics, none of the terms 'solid,' 'liquid,' 'supercooled liquid' completely defines the condition and properties of a substance in the glassy state. A glass is in fact a non-thermodynamic phase. Dr Jones and Professor Simon show that an understanding of the implications of this fact is essential both for the explanation of the unique properties of glasses and for an understanding of the Third Law of Thermodynamics.

The most characteristic property of a glass, and that which makes possible the familiar techniques of glass-blowing, moulding, and drawing, is that when it is heated it softens progressively. While the melting of a crystalline solid into a liquid is always accompanied by a sudden fall in the resistance to deformation, and by changes in all other physical properties, we may say that a glass loses its solid-like character gradually, by means of a continuous decrease in the value of the viscosity. Thus at room temperature the viscosity of a window-glass is so high that viscous flow is almost impossible to detect, and the most obvious quality of the material is its elasticity or rigidity. At higher temperatures, however, viscous flow becomes more and more apparent under the smallest stresses. As a matter of fact there is still elastic resistance to all types of deformation even at high temperatures, but this is elusive on account of the low viscosity.

A graphic illustration of the way in which the behaviour of glass changes continuously as it is heated is afforded by considering the properties of elasticity and flow. The curves of figure 1 show how the deformation (or strain) increases with time under, say, a constant shear stress at various temperatures [1]. At low temperatures, the behaviour under constant stress is just what we should expect from a solid, that is, the glass shows an immediate deformation, which then remains practically constant and is actually recovered on removal of the stress. At the higher temperatures represented, the most obvious property is the viscous flow, but the recoverable elastic deformation can still be detected. There is, however, an enormous decrease in the value of the viscosity as the temperature is increased, which changes the whole character of the curves. Thus the slight increase in free volume gives the atoms or molecules much greater freedom to diffuse or to change places, but without greatly affecting the average interaction between them.

The progressive softening or hardening has a more than purely practical importance: it is also the feature of greatest scientific interest. X-ray pictures show that the structures of glasses are quite similar to those of ordinary liquids, and we are thus enabled to study typical 'liquid' properties with relatively simple experimental techniques, since we have, as it were, a slow-motion model available.[1] Also, as we shall see later, we can isolate, or focus on, certain important properties in a way which is otherwise impossible, and

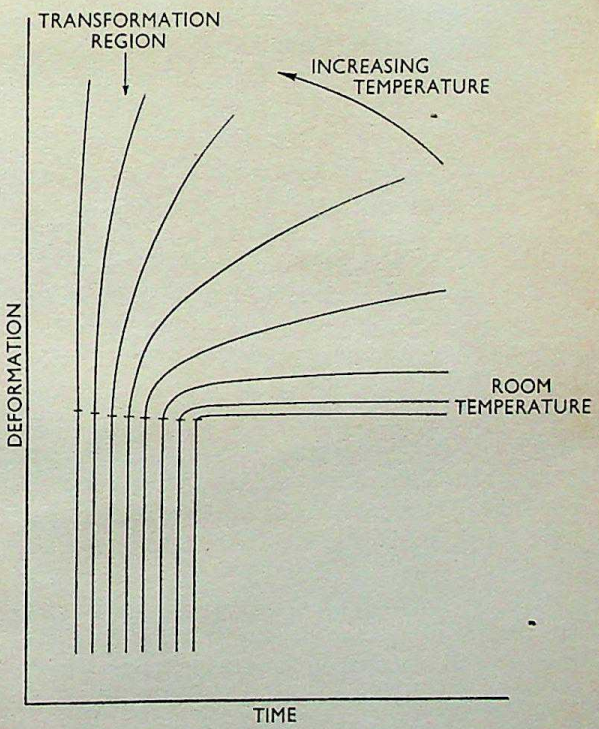

FIGURE 1 – *Deformation of glass under constant stress at differing temperatures.*

[1] For example, we may guess from figure 1 that the flow behaviour of a liquid probably does not consist only of Hookeian elasticity plus Newtonian viscosity, as assumed by Maxwell in his well-known equation of 'visco-elasticity.'

the results of these studies are of great theoretical interest. And, of course, the properties of ordinary glasses at room temperature—not all of them desirable—are determined by the kinetics of this hardening process.

THE THERMODYNAMICS OF GLASS

Let us first consider how glass is to be classified from a thermodynamic point of view. We shall for the present understand by the term 'glass' any substance formed by continuous cooling from the liquid condition such that its viscosity has risen to about 10^{13} poises or greater. The significance of this figure will be discussed later. (The viscosity of ordinary glasses at room temperature is actually much higher than 10^{13} poises, and they behave as brittle solids.) In the typical case this means that we have a liquid super-cooled below its freezing point and therefore not thermodynamically stable.

We might expect that the tendency to crystallize or devitrify—that is, to reach the state of lowest free energy—would be the most important problem in all studies on glass. This is not so, however. As shown by Tammann [2] and his school, the tendency to devitrify does not increase continuously as the glass is cooled below the liquidus temperature, but in the absence of artificial nuclei there is a fairly narrowly defined 'dangerous range' of temperature for devitrification, well below the liquidus temperature. (The viscosity at the liquidus temperature is usually about 10 poises, and at the dangerous range for devitrification about 10^4 poises.) It has generally been considered that this is because the two main factors affecting the rate of devitrification lead to effects which vary with temperature in opposite ways. Thus the free energy difference between solid and supercooled liquid increases as the temperature is lowered, but the viscosity, which resists the process, also increases rapidly. The theory has been developed and refined by Becker [3], Frenkel [4], and others to take account of the question of the stability of embryonic nuclei formed by thermal fluctuations—or self-nucleation. In all inorganic glasses which are of practical use and commercially made we are always well below this dangerous region, so that devitrification is of negligible importance and we need not consider it further.

The ability of a substance to super-cool and finally to form a rigid glass is determined by its structure in the liquid condition, and can very roughly be related to the viscosity, or to the activation energy constant (B) in the well-known relation ($\eta = Ae^{B/RT}$) between viscosity and temperature, derived by Andrade [5] and others. A high value of this activation energy means that the atoms or molecules cannot easily change their relative positions, and this is obviously some measure of the resistance to crystallization; it also means a high rate of increase of viscosity with falling temperature and thus a good probability of forming a rigid glass at some lower temperature.

Is glass then nothing more than a super-cooled liquid? The answer to this is 'No.' At sufficiently low temperatures all glasses show phenomena of a new and unusual kind, and we must consider these in detail because of their thermodynamic—and practical—significance. As was shown by Tammann [6], all glasses, super-cooled liquids, or other amorphous substances show rapid changes, at particular temperatures, in such properties as the coefficient of thermal expansion, and the value of the viscosity at this temperature is always found to be about 10^{13} poises. For a long time the significance of this clue was missed in spite of the fact that these anomalies occurred in such widely differing substances as glycerol (at about $-100°$), selenium (at room temperature), ordinary inorganic glasses (at 400°–600°), and fused silica (at about 1200°), and the suggestion was frequently advanced that glass below this transformation temperature, as it is usually called, was a 'fourth state of aggregation.'

The explanation was given by one of us [7] about 1930, following a series of experiments [8] concerning the general validity of the Third Law of Thermodynamics (Nernst's Heat Theorem). This law postulates that entropy differences between all states of a system disappear at absolute zero. Now since entropy is a measure of the degree of order, this would mean that at absolute zero a crystal and a glass should be in the same state of order. However, we know from X-ray studies that the atoms in an ideal crystal are arranged in the perfect order of a lattice, whereas the arrangement of the atoms in liquids or glasses has only a degree of short-range order.

Thus one could not see how the Third Law could be obeyed by such a system. In order to find out more about this point, the specific heat of glycerol was measured down to liquid-hydrogen temperatures (a little later the same substance was also investigated by Gibson and Giauque [9]). The results are shown in figure 2. We see that there is no discontinuity in the specific heat as we pass from stable liquid above the melting point to super-cooled liquid below, the value thus still being very

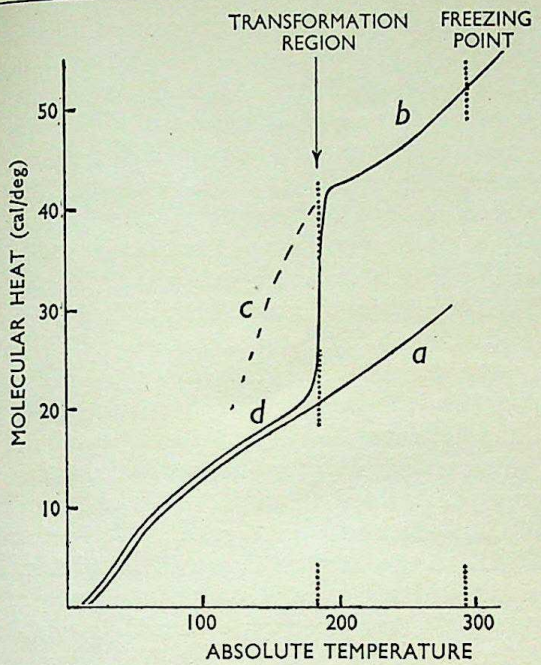

FIGURE 2 – *Molecular heat* (C_p) *of glycerol.* (a) *Crystal,* (b–d) *liquid, super-cooled liquid, and glass,* (c) *expected form of equilibrium curve for super-cooled liquid.*

much higher than that of the crystal. This state of affairs continues until about −100°, when a relatively sudden fall occurs, nearly to the value shown by the crystal. The region of the anomaly is the transformation temperature or, preferably, the transformation region.

From the data of these curves and the known heat of melting, it is possible to calculate the entropies of the two phases, and the entropy differences are shown in figure 3. It is obvious that the entropy difference between the liquid and

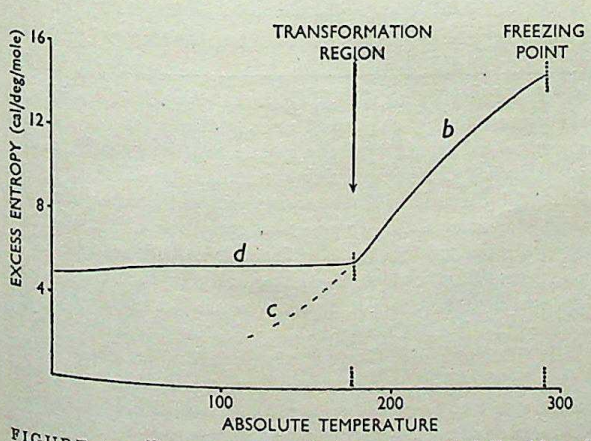

FIGURE 3 – *Excess entropy of the super-cooled liquid and glass over the crystal (glycerol).* (b) *Super-cooled liquid,* (c) *expected form of equilibrium curve for super-cooled liquid,* (d) *glass.*

the crystal does not drop to zero but remains nearly constant below the transformation temperature. Thus we seem to have a *prima facie* violation of the Third Law.

Does this behaviour actually constitute a violation of the law? The answer is given by the analysis of the specific heat curve. What is the significance of the high specific heat of the amorphous phase above the transformation region? We know that the viscosity is about 10^{13} poises at the transformation temperature. This corresponds to a Maxwell relaxation time[1] of the order of seconds or minutes, and suggests that the effect is in some way connected with atomic or molecular motions which are damped or restricted by neighbouring molecules.

One might thus imagine that the anomaly in the specific heat was due to the possibility of new degrees of freedom, such as would come into play if torsional vibrations could change into rotations above the transformation region. It can easily be shown, however, that not more than about a quarter of the total magnitude of the anomaly could be explained in this way.

The explanation is quite different. The entropy, or disorder, of a substance is made up of a number of contributions. First, there is the thermal motion (translational, vibrational, and rotational) in all states of aggregation. This is usually the only contribution in a gas, and also in a crystal, where the centres of the molecules are more or less fixed in lattice positions. In a liquid, however, things are different. Although at one time liquids were generally regarded as systems of complete disorder, we now know that they have a degree of short-range configuration order. The forces of attraction between atoms are order-producing, and also, as has been illustrated by Hildebrand [10] on the basis of a 'tennis-ball' model, the mere fact that atoms retain their impenetrability or mutual repulsion is enough to lead to a certain degree of order.

Now, disorder increases with temperature, and this fact contains the explanation of our specific heat anomaly. The change of configuration with temperature must have an effect on the specific heat, since we have to supply energy to increase the disorder, and it is actually mainly responsible for the fact that the specific heats of liquids are higher near their melting points than those of their corresponding solids. This contribution is

[1] Defined as the time in which the stress required to maintain a constant strain falls to $1/e$ of its original value through viscous relaxation.

not easily detected, because only relatively complicated liquids super-cool, and the values of their specific heats are too difficult to interpret. However, the fact that in the transformation region the mobility of the molecules disappears more or less sharply causes this contribution to the specific heat to drop out, and in doing so to reveal itself strikingly.[1] It is clear that this configurational specific heat, as it has been called by Bernal [11], is of essential significance, and no theory of the liquid state can be complete which does not account for it. Bernal's molecular theory of liquids, which is based on a number of simple assumptions and uses a semi-empirical model of liquid structure, contains a representation of this quantity, and he also shows how the equilibrium degree of order or configuration can be a function of temperature and pressure.

If this explanation is correct, the specific heat below the transformation region must be a function of time, and if sufficient time could be allowed for internal equilibrium to be continuously established when measuring the specific heat, it should follow a continuation of line (*b*), as indicated by the dotted line (*c*) in figure 2. To test this prediction, Oblad and Newton [12] carried out specific heat measurements on glycerol, in which times up to one week were allowed for the establishment of equilibrium.[2] Their values agreed well with those predicted, and they were able to follow the equilibrium curve to about 15° below the transformation region. The exact location of the transformation region thus depends on the time-scale of the experiments, and it appears at the temperature at which the equilibrium time of configurational adjustments crosses this time-scale.

By allowing still longer times for adjustment it should be possible to follow the dotted line to still lower temperatures and thus to still smaller entropy differences. Although a practical limit is very soon reached, it is safe to predict that, by an infinitely slow approach to the absolute zero, one would approach vanishing entropy differences.[3]

Thus the picture which we have is the following. In substances which can be super-cooled considerably, the properties of the super-cooled liquid are at first continuous with those of the stable liquid, the system being in *internal* equilibrium. In this condition the substance rests in a free-energy minimum, but not in the lowest possible minimum—that of the crystal. The mutual positions of the molecules are those of thermal equilibrium, and the state of the substance is completely described if we know the number and kind of particles and the temperature and pressure. Below the transformation region, however, the system loses its ability to readjust its configuration. It is for this state that we reserve the term 'glass' (a definition which accords well with the popular use of the term, since the great practical usefulness of glass arises from the fact that configurational changes in the material are extremely slow). In a glass, changes of temperature result, to a first approximation at least, only in changes in the thermal vibrations, which are more or less the same as in the crystal—the specific heat is actually slightly larger owing to the larger volume of the glass. A glass is not in internal thermal equilibrium. The system cannot be defined by stating the number and kind of particles and the pressure and temperature. We have already seen that slow cooling leads to

[1] It is important to realize that the relatively sudden drop in specific heat in the transformation region is in no way analogous or similar to the so-called 'lambda' phenomenon in the specific heat curves of substances which show order-disorder transitions. In our case the drop is due to the fact that internal equilibrium is *not* reached below the transformation region, while at all points on the lambda curve the substance is in internal equilibrium and the relatively sharp change is due to the development of a particular kind of co-operative phenomenon. Of course the *total* configurational entropy is the expression of a partial order-disorder transition, namely that between the state of order of the liquid at the absolute zero and its state of order at the melting temperature.

[2] An elegant experimental proof of the reality of the equilibrium in the super-cooled liquid has been given by Lillie [13]. By carrying out appropriate heat-treatments he was able to establish configurational temperatures both above or below a chosen temperature. When the temperature was then rapidly adjusted to this chosen value he was able to show that the viscosity (as measured) could approach its equilibrium value from either side.

[3] It can easily be shown from the thermal data already mentioned that the internal energy difference between the super-cooled liquid and the crystal will not vanish, and it is perhaps worth emphasizing that the 'equilibrium' glass formed by infinitely slow cooling will not become identical with the crystal. If we want to speculate about the configuration of this glass at the absolute zero, it may be useful to remember that one liquid actually exists for which an approach to the absolute zero can be realized experimentally, namely helium. Owing to the high zero-point energy of helium this liquid is more stable under its own vapour pressure than is the solid. Liquid helium, indeed, approaches the same entropy at absolute zero as solid helium—which is stable above 25 atmospheres pressure—in spite of a quite different arrangement of the atoms. In this particular case at least the loss of entropy is not due to the establishment of geometrical order, but order is set up in 'momentum space.'

values of the specific heat which differ from those obtained by rapid cooling, and there are many other manifestations of the non-equilibrium, some of which we shall discuss later. We may mention, for instance, Tammann's [14] observation that by super-cooling liquids under different pressures and then releasing the pressure one can arrive at glasses with considerably different volumes.

We have in actual fact a practically infinite number of possible (but not equilibrium) states of the system; the glass has always a tendency to move from the configuration 'frozen-in' at a temperature in the transformation region, and corresponding to equilibrium at that temperature, towards that which would correspond to equilibrium at the temperature of its surroundings. Of course, the times required become longer and longer the further we go below the transformation region. This is quite different from the behaviour of a super-cooled, and therefore unstable, pure crystalline phase such as white tin, or diamond. We know that although diamond is unstable under ordinary conditions, with respect to graphite, it nevertheless remains in the diamond configuration for practically infinite times, and such persistence of a metastable crystalline state is quite common. Such phases, however, are in *internal* equilibrium; each slight deviation due to fluctuations only leads back to the original state, since all neighbouring states are less stable. Each atom lies in a potential-energy trough, and the whole structure lies in a free-energy trough—though not the lowest possible. In the glass, however, fluctuations tend on the average to lead it away from the chance frozen-in configuration towards that corresponding to equilibrium. The atoms lie in potential-energy troughs of differing depths; there are always some in troughs of practically zero depth, or at least in troughs bounded on one side by walls of practically zero height. The structure as a whole thus no longer lies at the bottom of a free-energy trough, but is, so to speak, stuck at some point on one of its sides.

It is thus not the fact that a glass is a super-cooled, unstable phase which is characteristic for it, but the fact that it is a super-cooled *disordered* phase. It has a chance configuration, frozen-in at some temperature in the transformation range, and only one of a continuous series of possible disordered configurations.

We can of course apply thermodynamic considerations to, say, the transition from graphite to diamond, because we can think of a mechanism by which we could establish an equilibrium between the two states at any temperature—for instance by increasing the pressure [15]. The glass, however, is not in internal equilibrium; we cannot even think of any method by which we could establish an equilibrium between the glass and crystal and therefore be enabled to transform the crystal reversibly into the glass, at temperatures below the freezing-in region. In other words, we cannot, starting from a given temperature, aim at and reach the configuration corresponding to a higher temperature. Glass is not a 'thermodynamic' phase, and we cannot, for instance, apply the Second Law of Thermodynamics to calculate the vapour pressure, since a vapour pressure cannot build up unless configurational adjustments are possible, at least on the surface. Such a phase has no definite vapour pressure—it changes with time.

We can still speak of the entropy of a glass at the absolute zero from the statistical point of view,[1] just as we can speak of the entropy of a gas disturbed by ventilators. We cannot, however, expect to apply thermodynamic laws to these states, or at least to any properties connected with changes in the internal positions or orientations of the molecules. However, if we consider properties which are affected only by the vibrations of the molecules, such as the volume as measured over short periods, we can naturally expect to apply the laws of thermodynamics. Indeed, we find experimentally that one requirement of the Third Law, namely, the disappearance of the thermal expansion with the approach to absolute zero, is fulfilled.

Thus considerations arising from the Third Law of Thermodynamics have led us to a clarification of the nature of glasses. But the results of these investigations have also led to a clarification of the meaning of the Third Law. Previously, many scientists denied the Third Law any general validity [16]. We know now that entropy differences do not necessarily disappear between all conceivable states at the absolute zero, but only between those which are in internal equilibrium. Thus the Third Law is a general law of *thermodynamics*. One of us [17] has therefore given it the following formulation[2]: 'the contribution to the

[1] An estimate of this quantity was actually made by Pauling and Tolman [21] many years ago by the methods of statistical mechanics, that is, by considering the number of possible atomic configurations in the glass.

[2] This formulation has been accepted without essential change in the latest edition of *Statistical Thermodynamics* by Fowler and Guggenheim.

entropy due to each factor within the system which is in internal equilibrium becomes zero at absolute zero.'

Many similar systems are now known in which an arrangement stable at higher temperatures can be super-cooled, such as solid solutions, in which either an excess concentration of one component, or an abnormally high degree of disorder, can be retained by super-cooling. The ortho-para hydrogen system is another example. In modern low-temperature research we often come across systems in which some part, such as for instance the electron spin system, or the nuclear spin system, can correspond to a temperature quite different from that of the lattice vibrations. We can easily imagine systems, say a glass containing rare earth ions, and of course nuclear momenta, which could only be characterized by four different 'temperatures,' and a corresponding number of relaxation times.

The freezing-in phenomenon has more obvious and direct bearing in our case, however, than in most of the above examples. First, the quantities of entropy involved are larger. In the order-disorder transition in binary alloys, for instance, the total change in the configurational entropy is of the order of R (the gas constant) multiplied by the logarithm of a small number, while the changes with which we are concerned can go up to, say, R $\log_e 1{,}000$. Secondly, the change in order in liquids affects the whole structure of the material, whereas in the other order-disorder transitions mentioned the lattice points are more or less fixed, and it is only in the orientation or some other characteristic of the occupying atoms or molecules that there is disorder.

PROPERTIES OF GLASSES

We must now consider some of the practical implications of the unique position of glasses in the thermodynamic hierarchy. The most obvious and important fact is that an ideal glass is homogeneous to a much finer order of size than, for example, a polycrystalline metal. Formed by continuous cooling from the liquid, it possesses no 'structure' of greater size than that of the short-range order characteristic of a liquid. In other words, we can think of a lump of glass, just as of a single crystal, as being one large molecule. To this we can attribute one of the most important properties of glass—its transparency—since this must mean that there are no crystalline inclusions, and also no internal surfaces or holes, of size approaching the wavelength of light. It also affects the thermal conductivity profoundly, especially at very low temperatures, as Berman [18] has recently shown in the Clarendon Laboratory at Oxford.

We can also attribute the various mechanical qualities of glass—good or bad—to these facts, coupled with the fact that glass in ordinary use is not in internal equilibrium. The behaviour of glass under stress is analogous to that of an ordinary liquid, its yield point being at zero stress. Fortunately, however, the viscosity may be very high. There can be no slip along glide planes as in a single crystal, or as to a reduced extent in a polycrystalline material, but on the other hand these materials have the advantage of a very low rate of deformation, if any at all, below a critical value of the stress. It is therefore an interesting fact that glass is actually used as a *structural* material for applications which call for the greatest degree of rigidity, e.g. in the manufacture of the largest astronomical mirrors. Also, it is a matter of common experience that ordinary glasses are among the hardest of materials.

Naturally great care has to be taken to reduce to the minimum those effects which are due to the internal non-equilibrium. The configurational contribution to the value of any property usually has the same sign as the vibrational contribution, since an increase in either temperature means greater disorder.[1] A rapidly cooled piece of glass, which has a high configurational temperature, therefore has an abnormally large volume. It also has a relatively low value of viscosity, and a consequently more rapid rate of approach to equilibrium than slowly cooled glass. To achieve the greatest stability, therefore, the configurational temperature must be lowered as far as possible. Glass apparatus required for precision measurements, such as mercury-in-glass thermometers, is heated for a long time at a temperature somewhat below the normal transformation region for this purpose. In the case of optical glass it is particularly important that the configurational temperature should be the same everywhere, so it is essential that temperature gradients should be reduced to a minimum during cooling through the critical freezing-in region.

The very erratic behaviour of glass in respect of mechanical strength can again be attributed to the fact that it is, so to speak, one large molecule. It is generally believed that the breaking process

[1] This is not always true, and there are important exceptions to the rule in the behaviour of silica, water (which has recently been shown by the authors [22] to form a true glass), and certain alloys.

in all solids is precipitated by stress-concentration at flaws or weak places. In glass, a single crack starting at the worst flaw is able to spread right across the specimen. In a polycrystalline material, however, as pointed out by Orowan [19], it is difficult for a crack to break through from one crystal into a neighbour with different orientation, and the strength as determined is more of an indication of the average strength of all the crystals. There are also several possible mechanisms by which flaws can arise in glass which cannot play a part in crystalline material (though in this respect it has one advantage over the crystal, in which solidification occurs discontinuously). For instance, the fact that at room temperature ordinary glass has a configuration frozen-in from a much higher temperature (nearly three times as high a temperature on the absolute scale) means that the structure will contain 'holes' formed by thermal fluctuations which will correspond to the higher temperature [20].

The looseness of the essentially liquid-like structure of glass is also reflected in its porosity to sufficiently small particles, such as the smaller gaseous atoms and molecules, and sodium and other ions. This is made use of in the well-known glass electrode and in the manufacture of 'Vycor' glass. It is worth noting that the porosity below the transformation region can be reduced by prolonged heating, which tends to close up the structure.

CONCLUSION

Finally, a few remarks about states of aggregation. The glassy state has sometimes been called a 'fourth state of aggregation.' If we agreed to this definition we should have to class as additional states of aggregation many of the other examples mentioned above of frozen-in disordered systems. The lack of precision in this field is only due to the looseness of the definition of a state of aggregation. If we want a practical or popular definition, we can say that a solid body is something with which one can smash someone's head, a liquid is something in which one can drown, and a gas something which has to be kept in a completely closed container. From this point of view glass must certainly be classed as a very useful solid. Then there are definitions of the states of aggregation from purely molecular standpoints. The limits covered by the two kinds of definition certainly do not coincide. There are very soft crystal lattices and there are very hard disordered phases, such as the glasses. It is well known that a continuous change is possible between the liquid and gaseous states, and obviously in this case there can be no point in trying to define the exact limit of either 'state of aggregation'; this also invalidates any definition of the term 'state of aggregation' based on the existence of discontinuities between phases. Indeed, the possibility of a continuous series of states between solid and liquid cannot be excluded, although it has not yet been realized in practice. As usual, it is futile to try to force the whole variety of nature into the Procrustean beds of a few names. If we find difficulty in allocating glass to one of the conventionally defined states of aggregation it is not because we know too little about it, but because we know too much.

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The floor of the ocean

HANS PETTERSSON

Fuller knowledge about the floor of the ocean would enable geologists to explain much of the Earth's earlier history. Within recent years greatly improved methods of oceanography have been developed, and with the new core-samplers, hydrophones, and ultrasonic depth-recorders it has been possible to amass a wealth of valuable data. Professor Pettersson here describes some of the results obtained, especially those from the very successful *Albatross* expedition.

Some geologists have asserted—though with undue pessimism—that in a few thousand million years the Earth will have become completely desiccated and as bare of oceans as Mars is at present. Let us assume that this tragic fate—which will deprive our planet not only of its oceans but also of its oceanographers—has been half realized, so that the ocean surface has become sunk by about 2,000 fathoms. The Atlantic Ocean will then appear divided in two, the halves being separated by a mid-Atlantic continent, with a crest constituted by land which is now some 1,500 fathoms below the surface and is called by oceanographers the Central Atlantic Ridge. This is illustrated in figure 1, where the present continental surface is grey, the ocean remaining after the world-wide sinking of the sea surface is black, and the border-land left dry by the retreating water is white.

The deep ocean floor, which would still be under water after such a partial desiccation, is the least-known part of the Earth's crust, the *terra incognita* of oceanography, geology, and biology. Until 75 years ago it was practically unexplored; then the famous cruise of the *Challenger* (1872–6) threw it open to science. Owing to great technical difficulties, the progress made since then in studies of the ocean depths has been slow and laborious. As an example, we may take the sampling of deep-sea deposits by means of sounding tubes. During the half-century which passed between the expeditions of the *Challenger* and of the *Meteor* (the German Atlantic expedition of 1924–5), the maximum length of core raised from great depths increased only from two feet to three. This slow advance is the more to be regretted since the deep-sea sediments, accumulated through hundreds of millions of years, harbour a unique record of the main catastrophes—climatic, tectonic, and volcanic—which have passed over the Earth (figure 5). A close study of these archives of the deep would spread light over many obscure chapters in the Earth's past history.

During the second world war, Swedish oceanographers, cut off from active work at sea, devoted their efforts to improving the tools and methods used in studying the floor of the ocean. A first result was the vacuum core-sampler, which in 1942 gave us a core of 45 feet from the depth of the Gullmar Fjord. Three years later, Dr B. Kullenberg, by means of his piston core-sampler, succeeded in obtaining a core 65 feet long (figures 7 and 10). This was a sevenfold increase over the record length

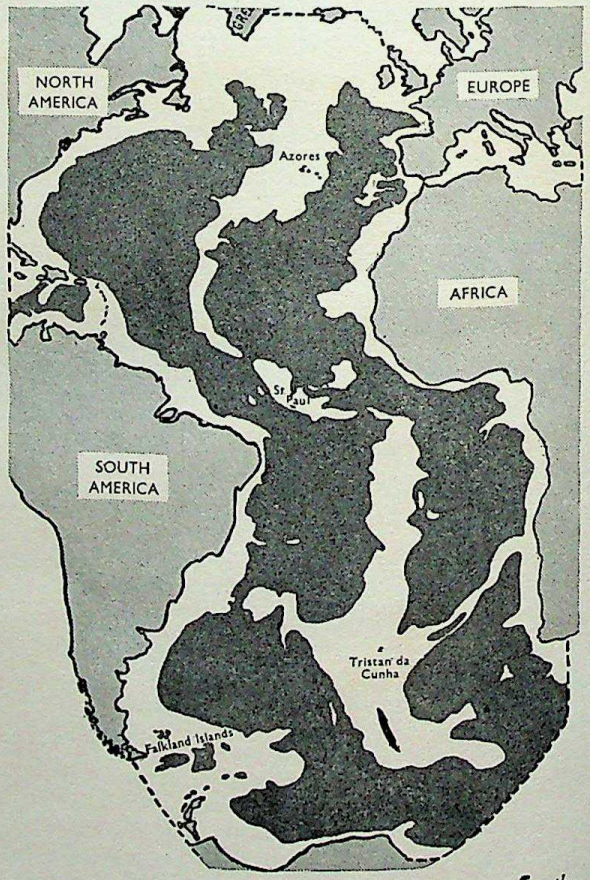


FIGURE 1 – *The Atlantic Ocean on a half-desiccated earth.*

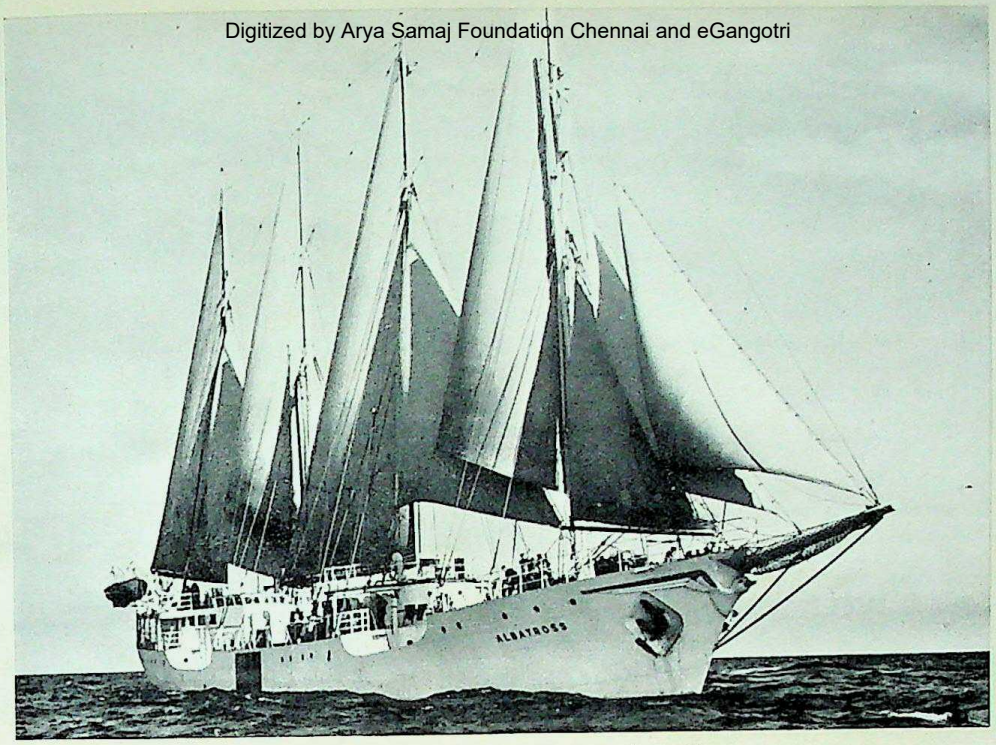


FIGURE 2 – *The* Albatross *under sail.*

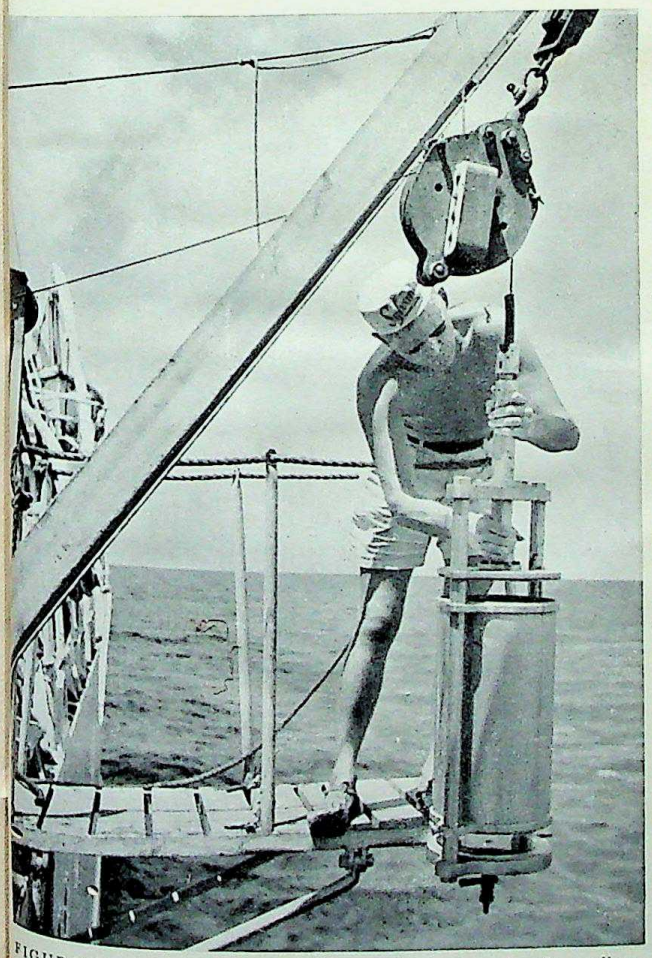


FIGURE 3 – *Large waterbottle for sampling sea-water for radium and uranium.*

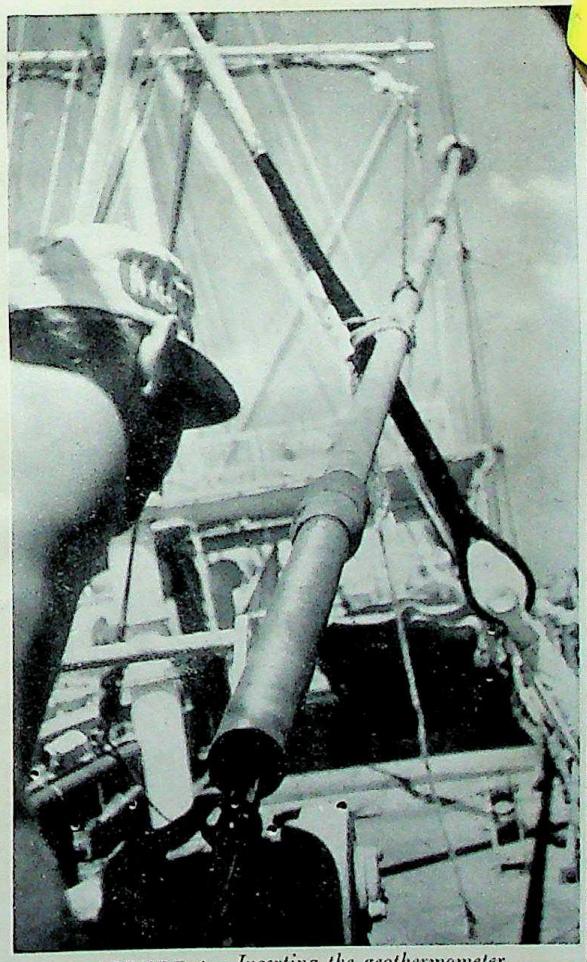


FIGURE 4 – *Inserting the geothermometer.*

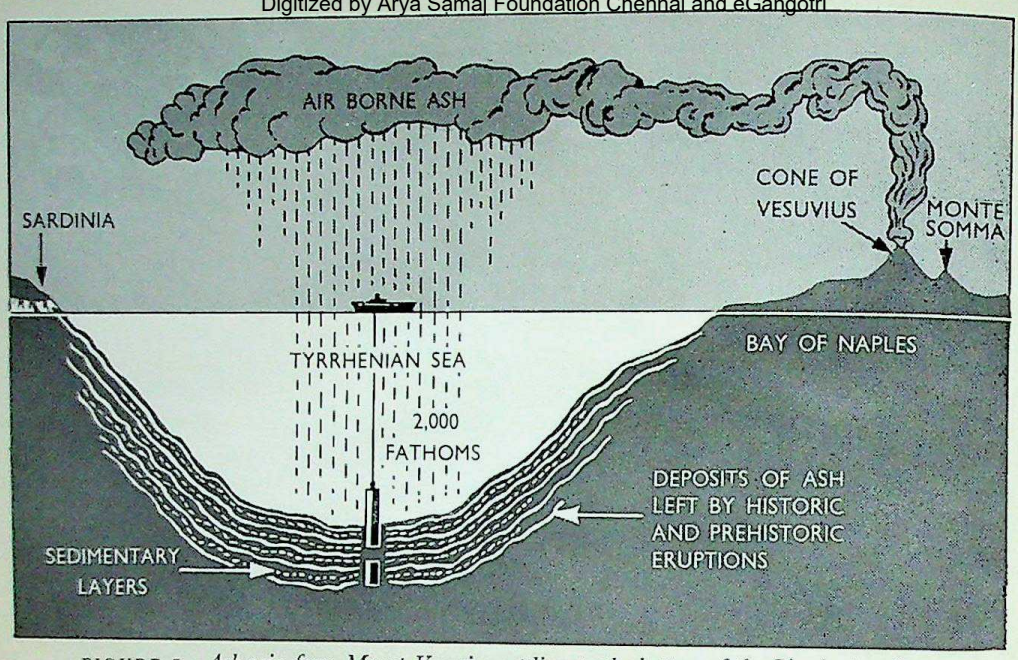


FIGURE 5 – *Ash-rain from Mount Vesuvius settling to the bottom of the Tyrrhenian Sea.*

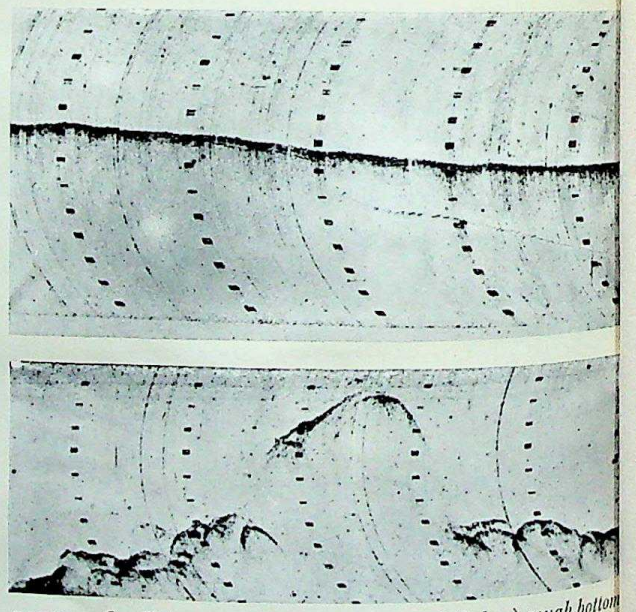


FIGURE 6 – *Echogram of (above) smooth and (below) rough bottom of the ocean in 2,500 fathoms. Depth scale 10 fathoms per scale unit; distance between two arcs about 1 nautical mile.*

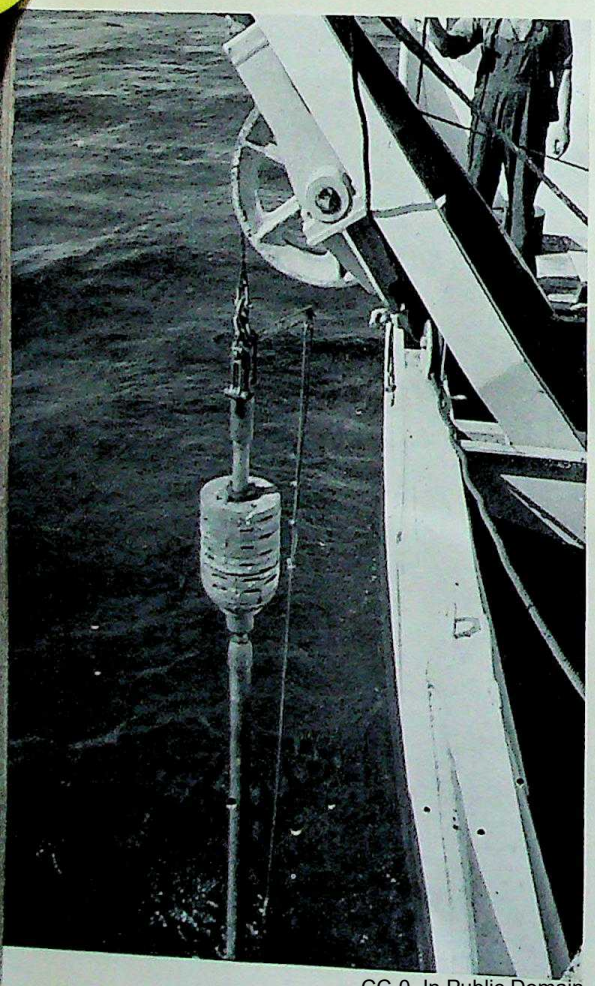


FIGURE 7 (*left*) – *The piston core-sampler ready to descend to 4,000 fathoms.*

of core obtained ten years earlier by means of an explosive core-sampler, invented by Dr C. S. Piggot. Figure 8 shows the development in core-length during 75 years. The span of time represented by the individual cores given in the figure is based on an assumed rate of accumulation of the Atlantic red clay of 7 millimetres in 1,000 years.

Another notable achievement was that of Professor W. Weibull, of the Bofors Armament Works, who succeeded in developing a method for measuring the thickness of the sediment carpet over the ocean floor. By recording, with hydrophones of special construction, the echoes from exploding depth-charges, reflected against the bottom and against the 'bottom below the bottom,' Weibull could locate reflecting surfaces covered by many thousands of feet of sediment. Other improvements were made in determinations of the radioactive elements uranium and ionium, present in seawater and in the sediments; in studies of the strength and the spectral composition of submarine daylight; and in investigating the occurrence of rare particles suspended in the water from great depths. A novel type of ultra-sonic depth-recorder was constructed for the Swedish expedition by a British firm (the Marine Instruments Company of London). Under favourable conditions of wind and ocean-swell, it drew a detailed curve showing the bottom profile down to depths exceeding 4,000 fathoms.

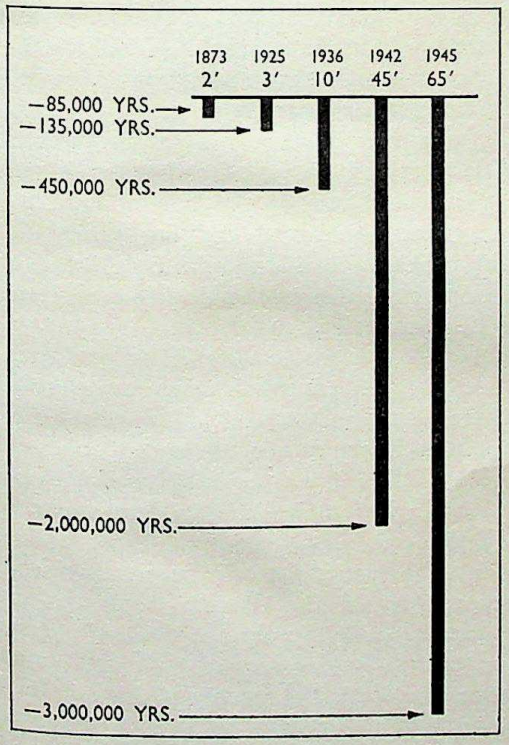


FIGURE 8 – *Diagram showing improvements in coring technique during the past seventy-five years.*

After a test cruise to the western Mediterranean in the spring of 1946, when the new technique was thoroughly tried out, the Swedish deep-sea expedition started on its circumnavigating cruise from Göteborg on 4th July, 1947. It was entirely financed by private donations given to the Royal Society of Göteborg, which sponsored the cruise. The splendid new training ship *Albatross*, a motor-schooner of 1,450 tons dead weight (figure 2) was lent to us, for our expedition of 15 months, by the Broström shipping combine of Göteborg on very generous terms. For the purpose of the cruise it had been converted into a floating laboratory at the Lindholmen shipyard (figure 11). A unique, very powerful, electrically driven deep-sea winch, with 4,400 fathoms of tapered steel wire rope made it possible to carry out coring and deep-sea trawlings with a minimum loss of time. Both operations were admirably conducted by Dr Kullenberg. The ship was under the command of Captain Nils Krafft. The scientific staff consisted of 10 to 12; they were specialists in the work to be performed.

Owing to the need for fair weather for working our very heavy gear the course to be followed was laid within or near the doldrums, where, fortunately, both the water layers and the sediments underneath present problems of very great interest; see the map in figure 9. In order to maintain a high standard of efficiency on the part of the staff in a tropical climate, the laboratories as well as the cabins and mess rooms were air-conditioned.

Following an almost straight course from Madeira to Martinique, raising long cores and sounding the sediment layers under way, the *Albatross* reached the Panama Canal six weeks after the start. On 27th August, 1947, the expedition set out from Balboa on its Pacific cruise, which lasted for nearly five months. A zigzag course was followed, which afforded opportunities of taking four complete oceanographic sections across the equatorial current system (figure 9). On the way, the Galapagos Islands, Nukuhiva (in the Marquesas), Tahiti with Papeete, and Oahu with Honolulu were visited, as well as the interesting atoll of Kapingamarangi. Attempts, partly successful, at measuring the unknown geothermal gradient in the deep-sea deposits were also made by means of a new geothermometer designed for great depths (figure 4).

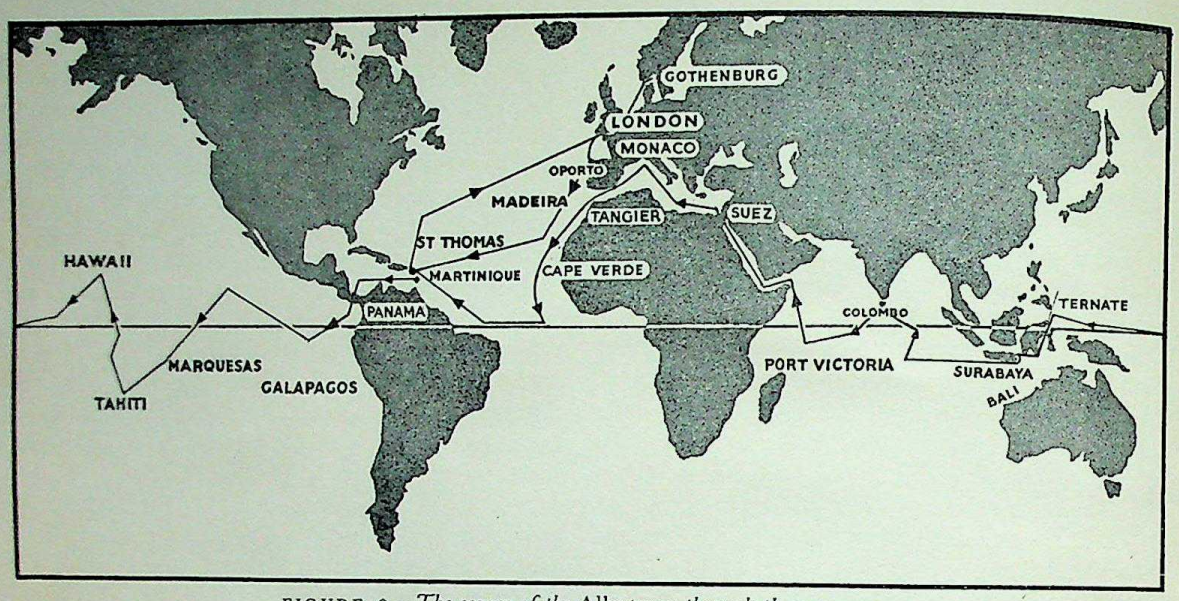


FIGURE 9 – *The course of the* Albatross *through three oceans.*

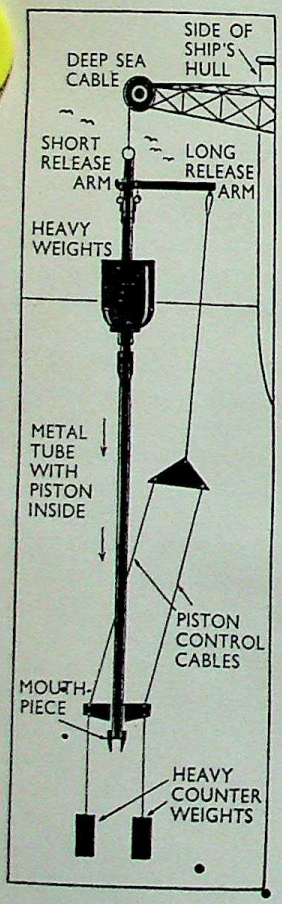


FIGURE 10 – *Schematic drawing of the piston core-sampler.*

After working in the great deep S.E. of Mindanao the *Albatross* passed through the Sunda Sea, with its many active volcanoes, to Surabaya, Java, and thence, via Bali, into the Indian Ocean. Here the only gale of the cruise occurred; it gave us four rather uncomfortable days. In the Indian Ocean the route lay mainly south of the equator, with a northerly detour to Colombo, and from there to the Seychelles, the 'Paradise of the Indian Ocean.' Proceeding through the Red Sea and the Mediterranean the expedition near the end of May 1948 reached Monaco, the Mecca of deep-sea research since the days of its great oceanographer Prince Albert I.

The last four months of the cruise were spent in the Atlantic Ocean, down to the Romanche Deep and St Paul's Rocks on the equator, and over to the Virgin Islands in the West Indies. During this part of the cruise Dr O. Nybelin, of the Natural History Museum of Göteborg, made rich catches of fishes and invertebrate bottom animals by means of the deep-sea trawl. His deepest haul, made to the N.E. of the Virgin Islands, proved that even at a depth of more than 4,200 fathoms organic life exists.

On our way back to Göteborg, where the *Albatross* arrived on 3rd October, 1948, we had the pleasure of visiting the Port of London and showing our equipment and our results to our British colleagues who visited the *Albatross*.

The main results gained during the expedition may be summarized as follows:

1. Down to the greatest depths encountered, the bottom profile is much more rugged than has generally been assumed, a large stretch of flat bottom being rather the exception than the rule. This fact is a serious complication, both in coring operations and in deep-sea trawling (figure 6).
2. Hard bottom is not of infrequent occurrence, especially in the Pacific and the Indian Oceans. It is largely an effect of submarine volcanism having spread extensive lava beds over the ocean floor, some of them covered by only a thin veneer of sediment.
3. Depth-charge soundings of the thickness of the sediment carpet gave much higher values in

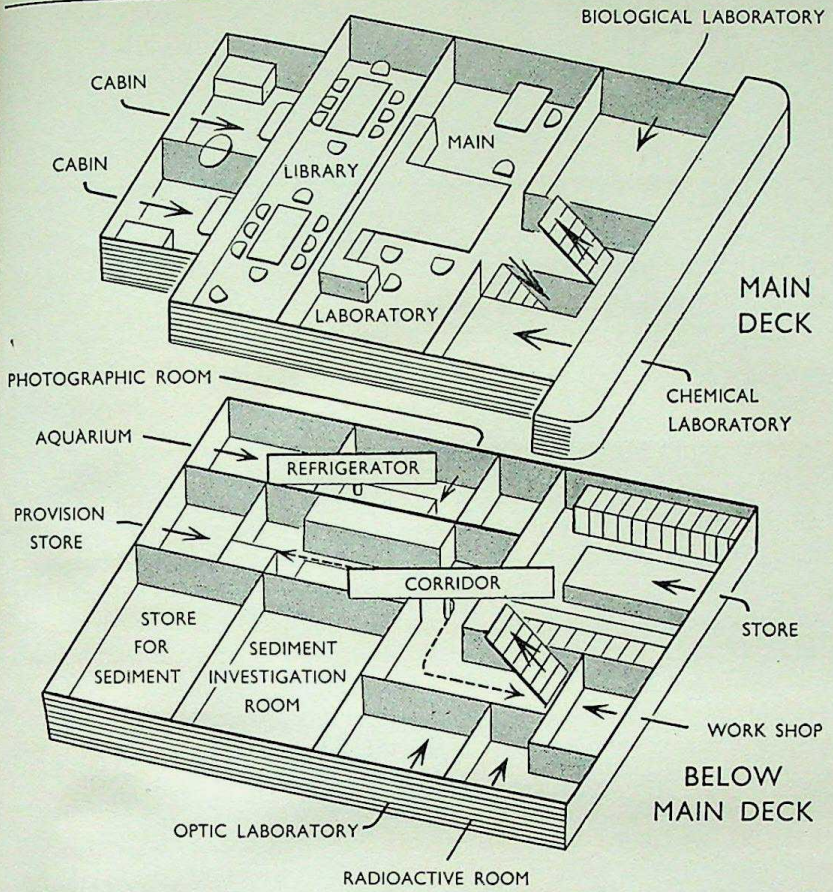


FIGURE 11 – *Plan of the laboratories in the* Albatross.

the Atlantic Ocean,[1] the Caribbean, and the Mediterranean, than in the Pacific and the Indian Oceans. It is possible that these latter results may be due to intermediate lava beds reflecting the explosion waves.

4. The sediment cores raised from great depths in all three oceans, ranging in length up to a maximum of 60 feet, made up a total length exceeding an English mile. They are now being subjected to various analyses in the laboratory. Even the cursory examination made on board showed many of them to be stratified, which indicates that variations in the conditions of sedimentation have taken place during the span of time represented by the length of the cores, from some ten thousand up to a few million years. Some of the changes are due to climatic variations, i.e. to the alternation of glacial and interglacial periods characteristic of the Quaternary Age. These variations can be followed by means of a biological analysis of the calcareous foraminifera shells found in different levels of the core. A surprising find was that of sand, or coarse mineral fragments, which blocked the core samplers both in the Mindanao and in the Romanche Deeps. Indications of 'slumping,' i.e. submarine land-sliding, were also encountered.

5. In the Mediterranean, the Caribbean, and the Sunda Seas numerous ash-layers from volcanic eruptions were found intercalated in the ordinary sediment. Organic remains and humus were of fairly frequent occurrence, especially in the seas just mentioned and in the open Atlantic west of St Paul's Rocks, as well as in the Bight of Panama.

6. A good catch of manganese concretions, some of them of considerable size, was made at a depth of about 3,000 fathoms S.E. of the Bermudas. Determinations of their rate of growth by measurements of the radium content are in progress.

When these abstracts from the records of the deep have been thoroughly studied by physical, chemical, radioactive, mineralogical, and biological analyses, much more will be known about the ocean floor and its deposits. It is to be hoped that this cruise, in which novel methods of deep-sea research have been successfully used, may be followed by others, and that the future study of the floor of the ocean will be based on international co-operation.

[1] The maximum value of nearly 10,000 feet would, with the assumed rate of the accumulation of red clay, represent a time-span of 300 to 400 million years, possibly still more.

Fruit development in relation to plant hormones

L. C. LUCKWILL

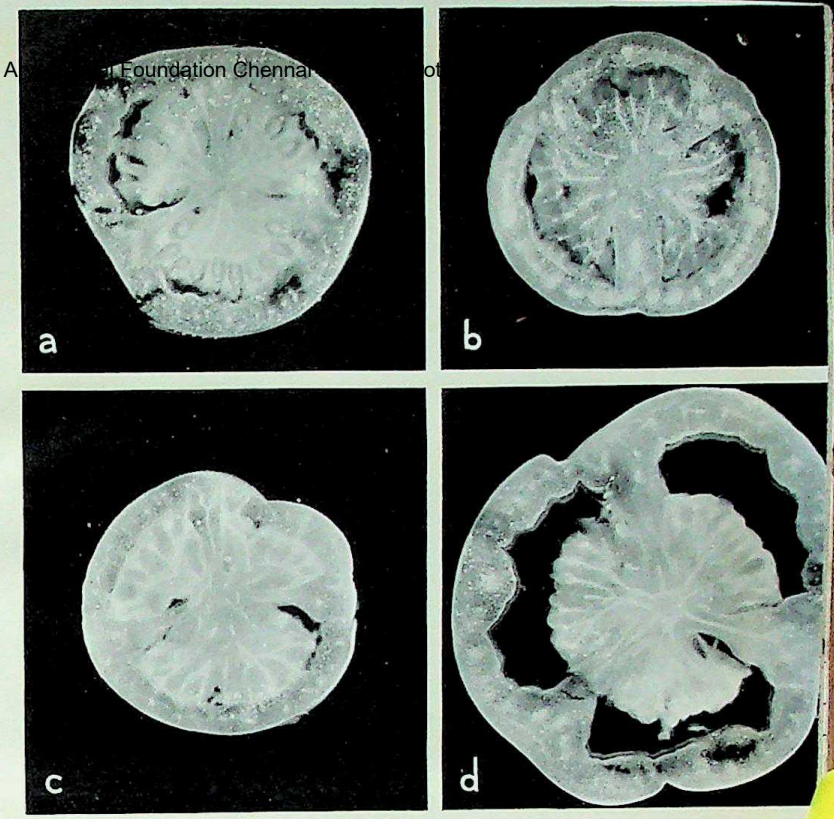
Recent work on plant hormones has shown that these substances play a vital role in the initiation and control of fruit growth. They are also known to control the process of abscission, which is the immediate cause of fruit-drop in apples and similar fruits. In this article, the importance of developing seeds as centres of hormone production in the fruit is stressed, and it is shown that appreciation of this importance has led to a fuller understanding of many previously known facts relating to fruit-development and fruit-drop.

The initiation of fruit-development in plants follows closely upon the act of fertilization. It manifests itself by a sudden renewal of growth in the ovary and adjacent tissues, the particular tissues involved varying widely in different plants. Thus, in the plum and tomato the fruit is developed entirely from the ovary itself; in the strawberry the edible portion of the fruit is derived from the floral axis, and the same is true for the apple and other pome fruits; in the mulberry and the pineapple it is the perianth segments of the flowers which enlarge and become fleshy; and in the pomegranate it is the outer coats of the seeds themselves.

The stimulus to growth which follows fertilization is now generally recognized to be hormonal in nature, though there is still some doubt as to the exact source of the hormone concerned. The pollen of many plants is known to contain growth hormones, and, as long ago as 1909, Fitting [1] at Buitenzorg demonstrated that aqueous extracts of the pollen of certain orchids were capable of inducing a limited amount of growth when applied to orchid ovaries. More recently, other workers have succeeded in stimulating fruit-development by injecting ovaries with extracts prepared from the pollen of quite unrelated species [2]. In nature, although a slight swelling of the ovary is sometimes observed after pollination, it is only in exceptional cases that pollination alone, unaccompanied by subsequent fusion of the male and female gametes, results in full development of the fruit.

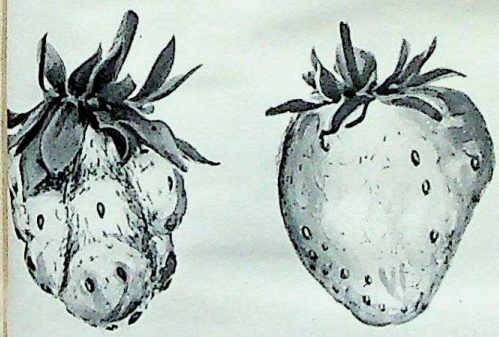
On the other hand, young seeds, shortly after fertilization, have been shown to be exceptionally active centres of growth-hormone production, and it seems very likely that it is this hormone which is responsible for the initiation of fruit-growth in many plants. In maize, no detectable hormone is present in the developing ovule, but immediately following gametic union hormonal activity appears, reaching its peak within ten to fifteen days and thereafter decreasing again [3]. A similar cycle of accumulation and disappearance of growth-hormone following fertilization has been observed in other cereals. In rye [4] and in apple [5] it has been demonstrated that the seed hormone originates, not in the growing embryo, but in the nutritive endosperm tissue of the seed. This tissue, like the embryo itself, is formed as a result of a sexual fusion in the embryo sac. In other plants, such as the tomato, the concentration of hormone in the young seeds is found to be very much higher than in other parts of the fruit [6], which again suggests that the seeds are the chief centres of hormone production.

That growth-hormones are in fact necessary for, and capable of stimulating, fruit-development has found confirmation in recent work on synthetic growth-substances. These substances are known to produce effects on growth similar to those produced by natural plant hormones, and, in certain plants, they are active in stimulating fruit-development in the absence of fertilization. A dose of only 0·001 μg of 2 : 4-dichlorophenoxyacetic acid applied to an unpollinated tomato ovary is sufficient to initiate fruit-development, and a dose of 0·1 μg results in the development of normal sized fruits. Other phenoxy- and naphthoxy-acids show similar fructigenic activity — though at somewhat higher dosage levels — and certain of these compounds are now widely used in commercial tomato-growing for setting the fruit under conditions when natural pollination is deficient. In the tomato, the fruits induced by growth-substances are seedless (figure 1), but in melons, *Datura*, *Melandrium*, *Oenothera*, and other plants, treatment with growth-substances stimulates not only the



URE 1 – *Transverse sections of tomatoes: normal seeded fruit produced by natural nation;* (b)–(d) *parthenocarpic fruits pro- d by treating unpollinated ovaries with* (b) *phthoxyacetic acid,* (c) *an extract of apple and* (d) 2:4-*dichlorophenoxyacetic acid.*

URE 2 (*below*) – *The effect of seeds on development is well illustrated by the berry. Where pollination is inadequate fertile seeds are formed and irregular mis- ben fruits like those on the left result. Notice the fruit flesh has swelled only in the areas acent to the fertile seeds. The fruit on the t has been sprayed with a synthetic growth stance* (α-*naphthalene acetic acid*) *which en- s full development of the flesh, even though seeds are present.*



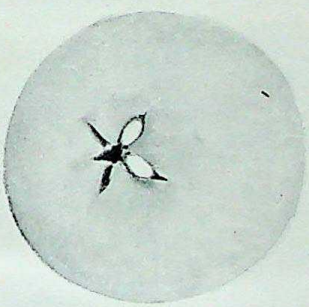


FIGURE 3 (*above*) – *Asymme- development of apples and ot pome fruits results from fail of seed development in one more of the five carpels.*

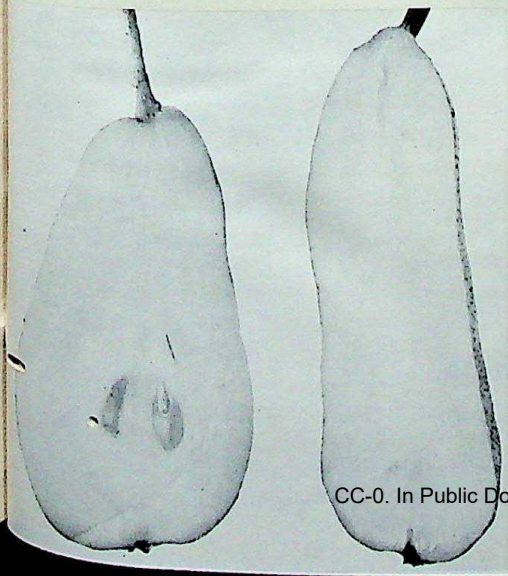


FIGURE 4 (*extreme left*) – *P thenocarpic* (*seedless*) *pears ar fairly frequent occurrence in m varieties, and differ markedly shape from seeded fruits of same variety.*

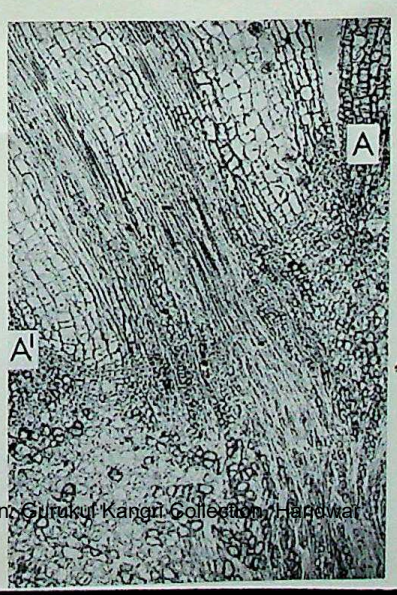
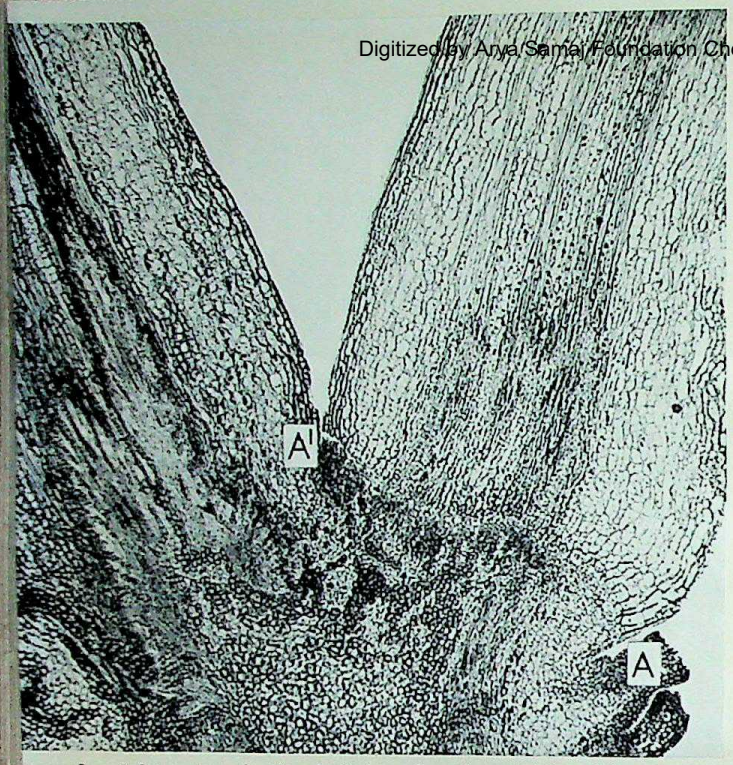


FIGURE 5 – *An early stage the abscission of a plum fruit A plate of meristematic c* (*A–A'*) *has formed across cortex and is spreading across vascular strands.* (*Magnifica* × 57.)



URE 6 – *A later stage in the abscission of a plum fruitlet. The abscission (A–A') extends across the base of the fruit stalk, and separation of the stalk the parent spur has already started at A'.* (*Magnification* × 37.)

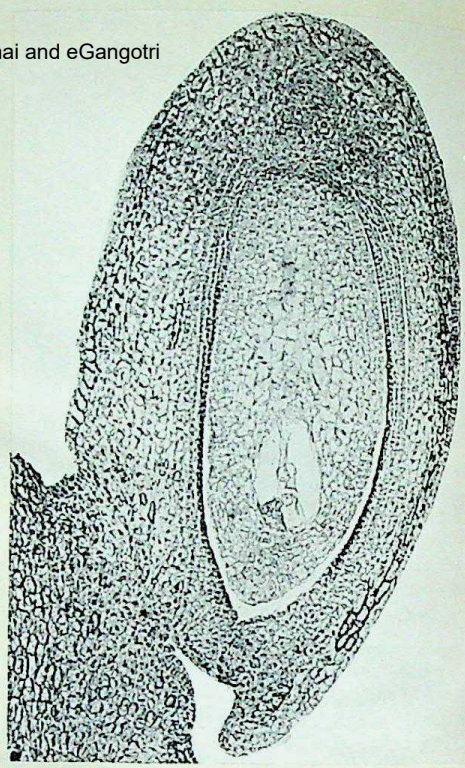


FIGURE 7 – *Longitudinal section of apple ovule the time of fertilization. In the centre of the embryo-s the fusion of one of the male gametes with the embry sac nucleus can be seen. It is from this fusion nucle that the hormone-producing endosperm tissue is d veloped.* (*Magnification* × 167.)

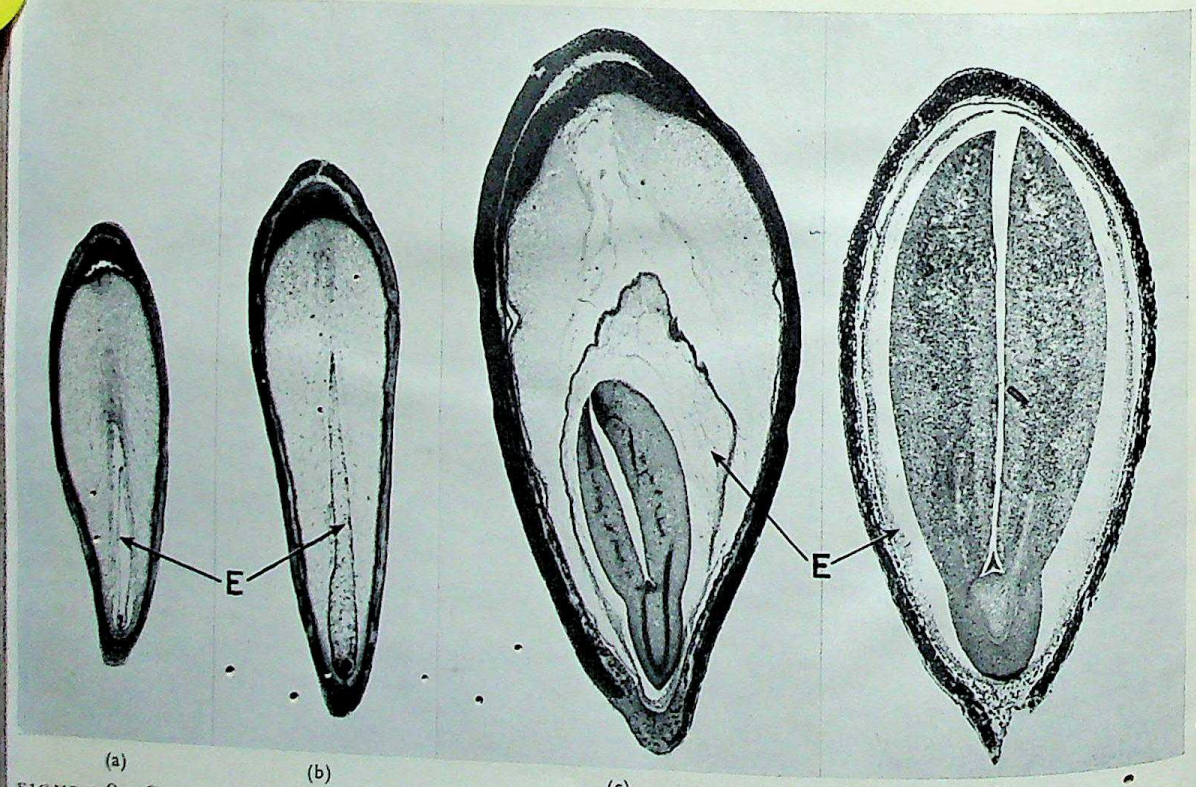


FIGURE 8 – *Growth of apple seed showing successive stages in endosperm development.* (a) *24 days after fertilization. The endosperm is still in the free-nuclear condition.* (b) *At 31 days the endosperm has become cellular and completely fills the elongated embryo-sac.* (c) *45 days. The endosperm is enlarging rapidly by meristematic activity at the periphery, but at the same time is being digested by the rapidly growing embryo.* (d) *76 days. The embryo is now fully grown and is enclosed in a sheath of active endosperm cells. E = endosperm.* (*Magnification* × 12.)

Figures 1 to 8 are reproduced by courtesy of the Director, Long Ashton Research Station

fruit but the seed coats [7]. Such seeds, although normal in external appearance, never contain embryos and are thus incapable of germination.

Although it seems that the hormone stimulus responsible for the initiation of fruit-development in many plants originates in the fertilized ovules, there are certain facts which suggest that this may not always be so. In the apple, for instance, no hormone can be detected in the young seeds until three weeks after the fall of the petals, yet during this interval the fruits swell rapidly [5]. Moreover, it is well known that some plants are able to form their fruits even though fertilization and seed development do not occur. This phenomenon, which is known as parthenocarpy, is particularly common among cultivated fruit plants, many of which have been specially selected for their ability to produce such seedless fruits. The banana, the Washington navel orange, and the Corinth (currant) grapes are well known examples. Even in plants which normally produce seeded fruits, parthenocarpy may occur spasmodically and may often be induced by external agencies. Conference and Fertility pears will often set a good crop of seedless fruits after the flowers have been damaged by frost, or when they are grown in a very warm climate, and seedless gooseberries, grapes, and apples have been produced experimentally by cincturing. In such examples, it is clear that the hormone responsible for fruit-development cannot come from the developing seeds, but must originate in the maternal tissues of the ovary or adjacent vegetative organs. Seedless varieties of oranges and lemons have been shown by Gustafson [8] to have an exceptionally high concentration of growth hormone in their ovaries, as compared with related varieties the fruits of which will develop only when seeds are present. This high hormone content appears to be adequate to ensure the continued development of the ovary into a fruit, even in the absence of seeds. The occasional occurrence of parthenocarpy, therefore, in no way invalidates the general hypothesis that the young seeds are the active centres of production of the hormone responsible for the initiation and control of fruit-development.

This hormone concept of fruit-development has thrown new light on several other phenomena for which there had previously been no satisfactory explanation. The influence of the seeds on the size, shape, and chemical composition of fruits has long been known; it is especially marked in apples and pears and other few-seeded fruits. A particularly striking correlation between seed number and fruit size is quoted by Müller-Thurgau [9] for grapes (figure 9), and similar correlations are reported for a wide variety of other fruits.

The influence of seeds on the shape of fruit is particularly well shown by the pome fruits, where failure of seeds to develop in one or more carpels results in asymmetric growth of the flesh (figure 3). In strawberries too, where only a few fertile seeds are formed, the swelling of the fruit is irregular, and is confined to the areas immediately adjacent to the seeds (figure 2). As in apples, the influence of the seed here seems to be strictly local in its effects. Parthenocarpic fruits often differ from seeded fruits of the same variety, not only in size and shape but in chemical composition. In pears, they are characteristically sausage-shaped (figure 4); in the Japanese persimmon they are smaller, earlier in ripening, and with darker flesh than seeded fruits of the same variety [10].

The phenomenon of metaxenia, or the influence of pollen on the character and growth of fruit, has for long been a subject of controversy among pomologists. Formerly, indeed, it was difficult to visualize how such effects could occur, since the fruit itself, with the exception of the content of the seeds, is entirely a product of maternal tissue. Many so-called metaxenia effects have, in fact, been shown to be due to somatic mutation, but

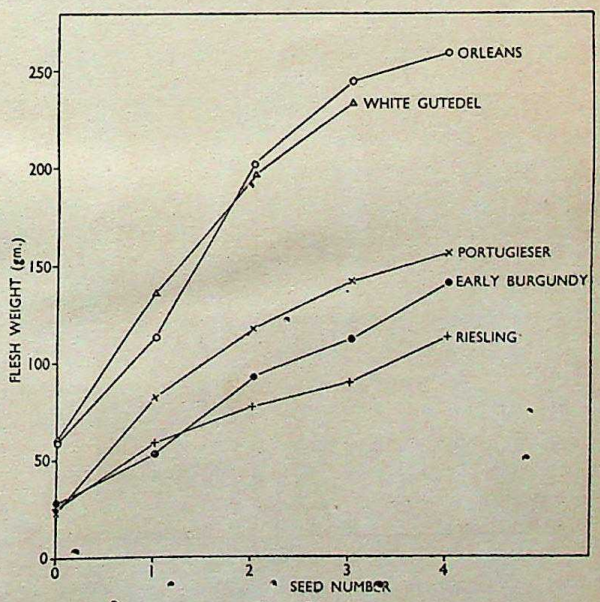


FIGURE 9 – *The correlation between seed number and fruit size is particularly well marked in few-seeded fruits, and is illustrated by the above graphs of flesh-weight in different varieties of grapes, based on the data of Müller-Thurgau.*

there nevertheless remain some well authenticated cases where the size, chemical composition, and keeping qualities of the fruit have been affected by the variety of pollen used. If it be accepted that fruit-development is under the control of a hormone produced in the seeds, the possible mechanism of such effects becomes apparent, since the quantity, and possibly the type, of hormone produced may well be influenced by the hereditary make-up of the endosperm, to which, of course, the male parent contributes.

In some plants it is usual for every flower which is effectively fertilized to develop into a mature fruit. This is so in the gooseberry, the cucumber, and the tomato. In species which flower abundantly and have large fruits, however, a large proportion of the fruitlets which start to develop are shed before they reach maturity. Such shedding is clearly necessary if impossible demands are not to be made on the nutritional and mechanical capabilities of the parent plant.

In the cultivated tree fruits the problem of fruit-drop is one of great economic importance, since the extent of the drop is often one of the chief factors determining the size of the harvested crop. In apples and plums, in which the phenomenon has been most intensively studied, the most characteristic feature of fruit-drop is its periodicity, successive waves of dropping being separated by 'sticking periods' during which few fruitlets fall. In the apple there are usually three waves of dropping: the first, or post-blossom, drop occurs soon after petal-fall, and is followed after an interval of one to three weeks by the so-called June drop; finally comes the pre-harvest drop, which, as its name suggests, is the fall of nearly ripe apples. In plums, too, three waves of fruit-drop can usually be recognized [11], though these are not necessarily homologous with those in the apple. From the economic standpoint, the early waves of fruitlet shedding are to a large extent desirable, as they represent a natural thinning-out of overcrowded fruit spurs, a process which otherwise would have to be carried out by hand. In some varieties, however, excessively heavy June drop frequently occurs, with consequent poor cropping, whereas in others the pre-harvest drop regularly accounts for large losses to the grower.

The separation of young fruitlets from the parent spur is an abscission process essentially similar to that responsible for the fall of leaves in the autumn. The first stage in the abscission of a fruit is the formation of a plate of meristematic cells across the base of the fruit stalk, or, occasionally in plums, at the base of the fruit itself (figure 5). This abscission layer, which may be anything from two to ten cells in thickness when fully formed, extends across all the living tissues of the stalk. The xylem elements which pass through the layer are stretched like a spring, and often break, leaving fragments within the zone (figure 6). The actual separation appears to be due primarily to chemical changes in the cell walls within the abscission zone, the cellulose of the wall changing into gelatinous pectic compounds. This results in a zone of weakness which is readily ruptured by the mere weight of the fruitlet. The scar left after the fruitlet has fallen is soon healed over with corky tissue developed from a secondary cambium below the original absciss layer [12].

Although the anatomical features of the abscission process are fairly well understood, the physiology and the underlying causes of fruit-drop are still only imperfectly known. The earlier pomologists laid stress on the importance of water relations, and Langley [13] in 1729 wrote:

'Tis very easy to conceive, that if very dry Weather exhales away that Moisture which is necessary for those Formations (the internal parts of the fruit, such as the kernels, stones, and

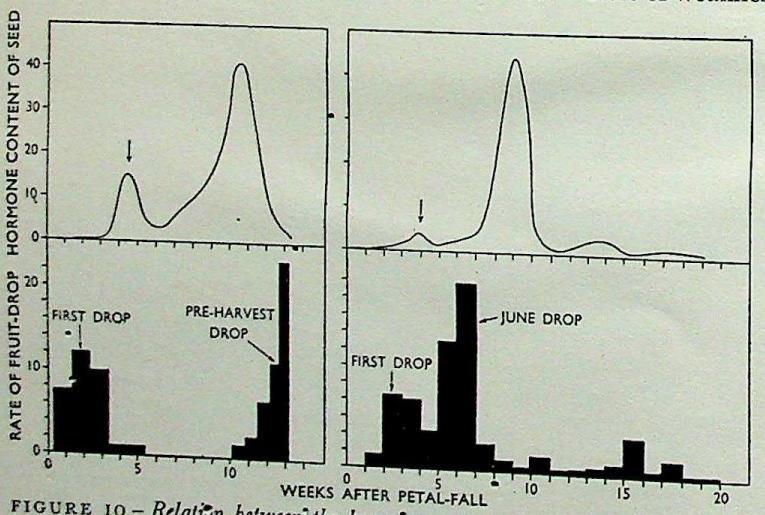


FIGURE 10 – *Relation between the hormone content of the seed and the rate of fruit-drop in the apple varieties Beauty of Bath (left) and Lane's Prince Albert (right). It will be noticed that the main peaks of hormone production are associated with periods of low fruit-drop. The arrows mark the stage at which the endosperm tissue becomes cellular.*

the like) the Work will be imperfect, and consequently the Fruits must perish.'

Since the days of Langley, much evidence has accumulated to show that restricted water supply during the early stages of fruit growth does, in fact, promote abscission; but, at the same time, it has become clear that water is only one of many factors which influence the drop. Nutritional factors also are of great importance, and a number of investigators have drawn attention to the close correlation which exists between the leaf area of the fruiting spur and the number of fruitlets which are retained. More recently, work on plant hormones has opened up a new aspect of the phenomenon of abscission, and seems to have brought the problem one stage nearer its final solution.

In many plants, it can readily be demonstrated that the formation of an abscission layer at the base of the leaf stalk is under the control of a hormone-like substance manufactured in the leaf blade. Removal of the leaf blade results in the rapid formation of the absciss layer at the base of the stalk, but, if the cut end of the stalk be supplied with growth substance, abscission is prevented. A similar experiment can be performed with apple fruits, suggesting that here, too, the abscission process is under hormone control. Growth substances applied in the form of sprays are also effective in delaying fruit-drop, and α-naphthalene acetic acid in particular is now widely used by growers for reducing the pre-harvest drop of apples and pears.

The importance of the developing seeds as centres of growth-hormone production has already been stressed, and the question therefore arises as to what part, if any, this seed hormone plays in the prevention of fruit-drop. Heinicke [14] found that apples with the fewest seeds tended to drop the most readily, which led him to suggest that the developing seeds have a pulling power for water and sap enabling those fruits with the greater number of seeds to develop at the expense of other fruits with smaller food-attracting abilities. In the light of modern knowledge, a more probable explanation seems to be that such fruits remain attached because, on account of their higher seed content, they produce more growth-hormone than fruits with fewer seeds. This supposition has recently been strengthened by direct measurements of the hormone content of seeds from dropped fruitlets and attached fruitlets in a number of apple varieties. Not only do the former contain fewer seeds, but the hormone content per seed is lower than in those fruits which do not fall [5].

There appears also to be some correlation between the variations in hormone content of apple seeds throughout the season and the successive waves of fruit-drop, particularly during the early part of the season [5]. In the varieties so far investigated, the main peaks of hormone production are found to coincide with 'sticking periods' when few fruits fall from the tree; conversely, periods of heavy fruit-drop are associated with low hormone production by the seeds (figure 10).

The wide fluctuations in hormone content throughout the season are themselves closely correlated with developmental changes within the seed, particularly with the growth of the endosperm, which, as already mentioned, is the chief hormone-producing tissue of the seed. The apple and related fruits are unusual in that the endosperm remains in a free nuclear condition for a period of some three to four weeks following fertilization (figure 8). During this period the seeds manufacture no hormone and abscission readily occurs. This first wave of fruit-drop is terminated by the formation of a cellular endosperm tissue (figure 8 b) and the simultaneous production of hormone. Subsequent partial digestion of the developing endosperm by the rapidly growing embryo causes a further temporary fall in hormone production which, in some varieties, seems to be associated with the June drop. On the completion of embryo growth, hormone production again rises and fruit-drop ceases.

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Electroencephalography

W. GREY WALTER

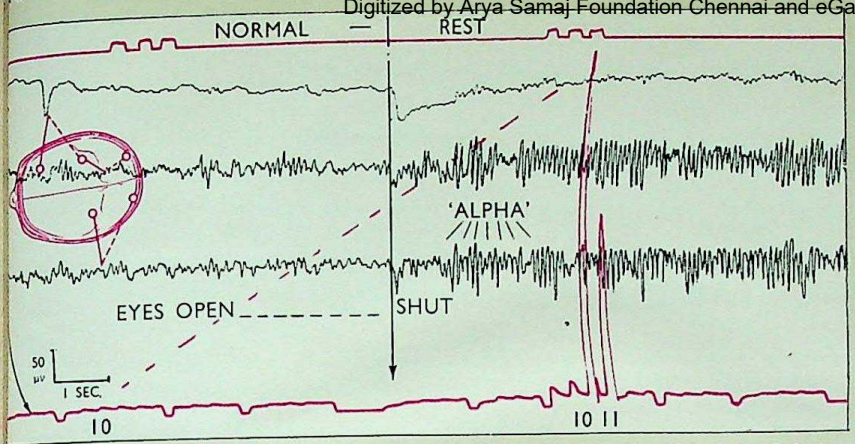
The human brain is more complex than any other known structure in the universe, and science can still do little except grope at unravelling its complexity. However, modern work on radar and the like has opened up a promising line of approach to the subject, and a new branch of science, electroencephalography, has been born. Dr Grey Walter, a pioneer in this field, describes the latest advances, and shows how some of the results may be interpreted.

The classical philosophers took so little interest in the brain that they referred to it merely as 'the thing in the head.' Until the last century it was considered as providing a sort of radiator for overheated animal spirits; only in the last generation has the study of brain-function developed into a serious science. Microscopical examination of the brain tissue revealed that it contains about 10^{10} nerve cells arranged in complex and systematic three-dimensional patterns. Electrical stimulation of the exposed brain and observation of the resulting movements and subjective sensations demonstrated the anatomical connection between some parts of the brain and various regions of the body, and it was found that, even when inactive, the brain consumes an enormous quantity of energy in relation to its size. Only in the last twenty years, however, has it been possible to study any aspect of brain function directly in the intact human subject. It had been known for a long time that communication between individual nerve cells is maintained by brief electro-chemical discharges along nerve fibres, but it was not believed that the electrical activity of the brain could be detected without placing electrodes directly on the exposed nerve-tissue until Berger demonstrated this possibility in 1928. A record of the electrical brain activity obtained in this way with electrodes on the scalp is called the electroencephalogram or E.E.G.

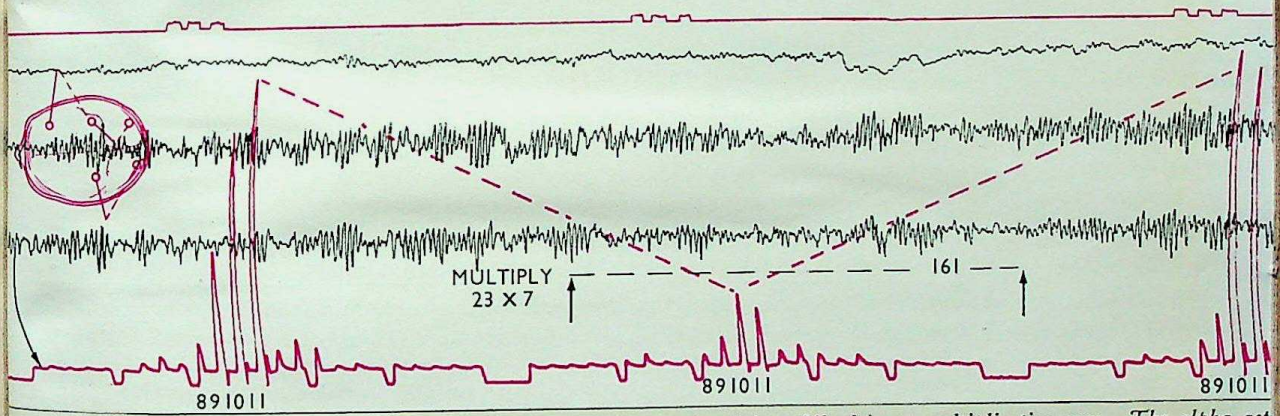
Such records show continuous electrical activity of an extremely complex nature, consonant with the huge number of nerve cells and the intricacy of behaviour patterns. As recorded through the scalp and skull, the potential differences of the electrical discharges are only a few millionths of a volt and have to be amplified with specially designed electronic devices which convert them into a continuous graph drawn on paper. The possibility of studying the normal brain in this way encouraged both clinical developments and the theoretical consideration of brain function as a whole. Present concepts can be summarized most concisely by stating that the general function of the brain is to construct and contain a working model of the outside world, and to test upon this model the effect of the operations which circumstances suggest are necessary for comfort or survival. The more accurate and detailed the model, the more trustworthy will be the forecast of the results of action, and the better the chances of survival of the organism. In the human brain, the working parts of the model are the circuits which link the nerve cells; since their permutations are of the order of $10^{10,000}$ there seems ample scope for detail—and for fantasy.

The notion of the brain as a signal analyser and statistical predictor has developed parallel with the design and construction of the various large computing engines sometimes known as electronic brains, but it must be admitted that as yet very little is known of the precise manner in which the animal brain composes its models so that they are compact enough to be portable, plastic enough to be changed from second to second, yet durable enough for a lifetime. It may be mentioned, however, that in man the purely nervous model is totally inadequate for social life, and is supplemented by external patterns in the form of written records, laws, and so forth. The neurophysiologist, then, would use the term 'mind' as meaning the individual's model of his environment and 'thought' as a miniature rehearsal for action. Such generalizations are bound to reawaken many ancient philosophical controversies, but have the virtue of promising linkage between brain physiology and other human interests, some of which will be considered later.

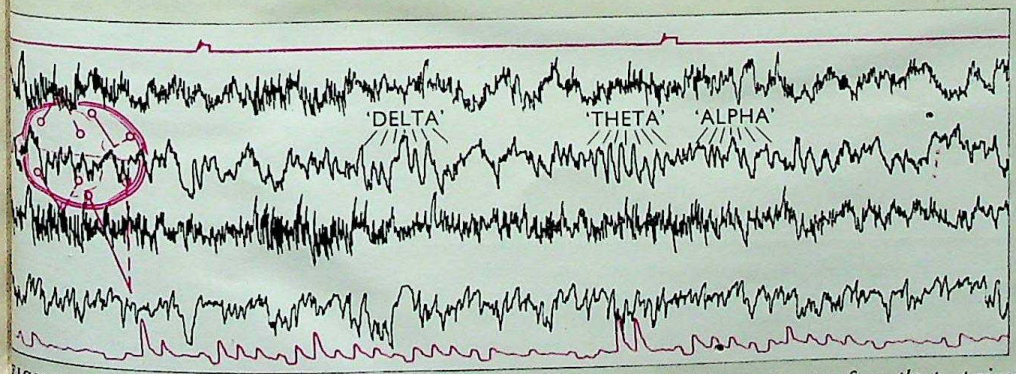
Returning to the discoveries in the field of electroencephalography, it was found at an early stage that recognizable perturbations of the electrical patterns occur in diseases of the brain. This observation had the unfortunate effect of distracting



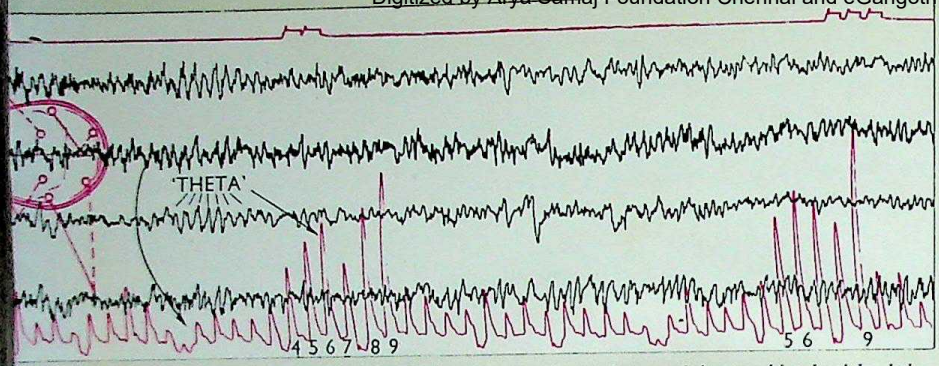
GURE 1a – *Electroencephalogram from a normal person showing the effect of closing eyes. Note the increase in alpha activity at 10 cycles per second in both occipital regions d the associated peak at 10 in the frequency analysis (shown in red).*



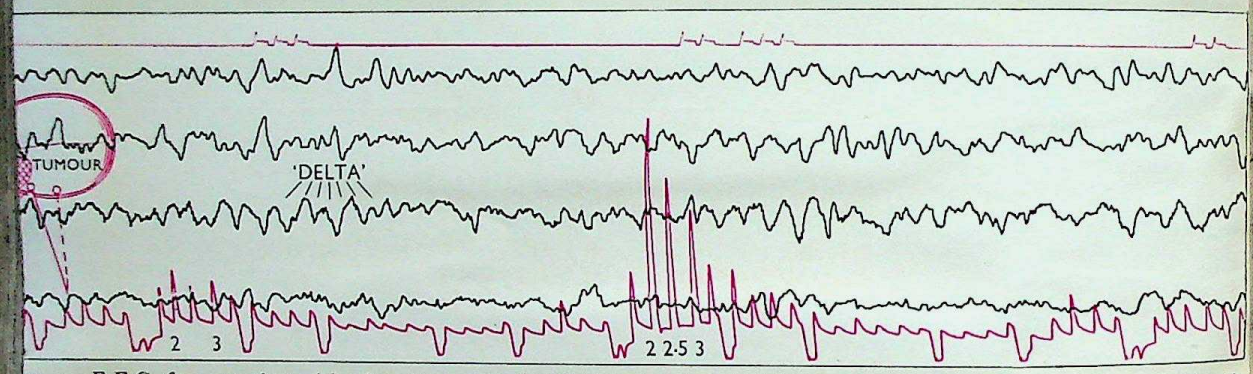
GURE 1b – *E.E.G. from a normal person showing the effect of mental activity while doing a multiplication sum. The alpha act duced and the extent of the reduction is indicated by the smaller size of the peaks at 8, 9, 10, and 11 cycles per second in the anal*



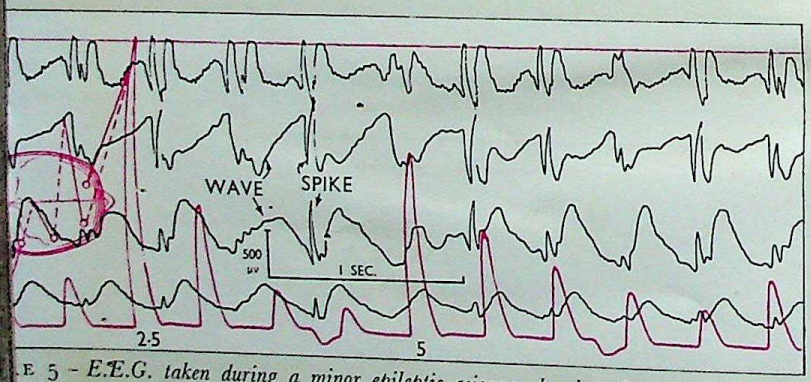
IGURE 2 – *E.E.G. from a one-year-old child showing delta, theta, and alpha components from the posterior egions. The analysis is from the frontal areas and demonstrates the absence of consistent rhythmic activity.*



E 3 – *E.E.G. from a three-year-old child showing prominent theta activity combined with alpha. ar record might be found in an adult with marked aggressive tendencies.*



E 4 – *E.E.G. from a patient with a large tumour in the left frontal region which is generating the large slow delta waves. Note the t 2, 2·5, and 3 in the analysis from between channels 2 and 3 showing where the slow waves are coming from.*



E 5 – *E.E.G. taken during a minor epileptic seizure showing the prominent 'wave ke' activity diagnostic of this condition. Note that the time scale is longer than in the cords and that the amplification has been greatly reduced.*

attention from fundamental problems, so that most laboratories engaged in this sort of work were soon full of records from epileptics and patients with brain tumours, and, during the war, with head injuries and abscesses. The literature of the subject contains thousands of papers and reports describing empirical correlations between various E.E.G. features and brain diseases, but of these publications only a few dozen are of fundamental importance, and there is no doubt that the great discoveries are still to be made.

Records from normal people show a great variety of more or less irregular electrical discharges from all parts of the brain, but in most subjects, when the eyes are shut, the discharges become more rhythmic in the occipital region, where visual impressions are projected. These regular oscillations are known as alpha rhythms and have a frequency of between 8 and 13 cycles per second. Even with the eyes shut, some alpha rhythms are usually diminished when the subject thinks hard, and some are blocked when a vivid visual image is called up. There is wide variation between individuals, but the general picture in a given subject is very constant and is almost like a signature (figure 1). It is important to note the paradoxical inverse relation between the prominence of the alpha rhythms and the level of functional activity and attention. In babies, there is little alpha activity; there are only much slower swings of electric potential in all areas (figure 2). In older children, rhythms at about 6 cycles per second are prominent up to the age of 7 or 8 (figure 3), but the alpha rhythms are beginning to appear, and the adult pattern is usually established by the age of 12. The 6 cycles per second activity is sometimes called theta rhythm; it is often larger when the child is unhappy or angry. It comes from the temporal lobes of the brain and deeper regions, and is found in many adults whose behaviour is childish in the sense that they are short-tempered, aggressive, and hard to get on with.

In sleep, the alpha rhythms disappear first, and the E.E.G. becomes less individual. In deep sleep it resembles a baby's record, but in lighter sleep there is usually intermittent activity at 14 cycles per second, and this is sometimes prominent just before a subject wakes up from a dream. Hypnosis produces little change unless the subject is of the type who goes into a very deep trance, when the alpha rhythms are said by some to respond to the suggested, rather than the real, conditions.

When the brain is injured, or invaded by a tumour, the affected area tends to develop slow discharges called delta activity (figure 4). Although they are usually localized round the lesion, these slow, abnormal delta waves are quite similar to those found in infants and deep sleep, suggesting that they may have some function in assisting the disturbed nervous tissue to rest from its labours, in the same way as pain compels disuse of a broken limb—for the brain can feel no pain, and has little power of healing itself.

The most dramatic variations from the normal are seen in epileptics, particularly during seizures. In *Petit Mal*, for example, when the patient suddenly becomes unconscious for a short time, the whole brain generates enormous regular slow waves a hundred times bigger than any normal rhythm, each one with a short spike indenting its crest (figure 5). One may consider a patient generating these 'wave and spike' rhythms, as they are called, as being electrocuted by his own brain.

Though always interesting and sometimes useful in the study of organic brain disease and epilepsy, the technique of electroencephalography has been too crude to give much help in problems of mental disorder, or in the investigation of the physiology of behaviour. In the last few years, however, the technical resources available to electro-physiologists have been greatly extended by the adoption and adaptation of devices developed during the war for radar or 'servo' machinery. Some new instruments, on the other hand, have been specially designed by those working in the field for their own peculiar problems.

The advance has been made on two fronts: first, the development of elaborate and flexible methods of transformation and display of the electrical data; second, the introduction of controlled stimulation of the subject. It will be realized that the ordinary record is really a graph of voltage against time, but since there are inevitably large numbers of cell-groups active at the same moment, this graph is nearly always extremely complex and bewildering to the eye, which can pick out only one or two of its many components. An instrument has been designed, and is now in use in many laboratories, which automatically breaks down the complex oscillations into their various constituents, rather as a spectroscope resolves white light into its component colours. This wave analyser writes out on the ordinary record every ten seconds a frequency histogram corresponding to the Fourier transformation of the primary changes. A mathematician would take several days to perform the same

task. Another device, still under development, displays the electrical activity on a battery of twenty-four cathode-ray tubes, each one corresponding to a small area of the brain. In this 'toposcope,' voltage is transformed into the brilliance of the cathode-ray screen, and an indication of frequency is given by the way in which the patch of light seems to rotate on each tube.

Ten years ago these devices would have seemed absurdly elaborate: in another ten year's time they will probably seem childishly simple compared with the intricacy of brain function as represented by the E.E.G. Even now, we can probably understand less than 1 per cent. of the total information contained in a record such as those in the figures. We are rather in the position of a visitor from Mars who is deaf and dumb and has no conception of the nature of sound, but is trying to build up a knowledge of languages by looking at the grooves on a gramophone record.

In dealing with a complex signal, there is always the problem of deciding how the significant parts of the message can be made most clear and memorable and the insignificant ones least obtrusive. Success in this discrimination depends upon choosing the right criteria for significance, and this can often be done only empirically until the cipher has been broken, so to speak.

The second sign of progress is that a more active approach is being made to the brain by providing controlled stimuli instead of merely watching its spontaneous activity. An analogy for this is the development of radar, in which instead of trying to pick up the sound or radiation from an aeroplane, a radio pulse is transmitted towards it and the echoes produced are observed in relation to the original signal. In the study of the brain the transmitted signals are called stimuli and the echoes responses, but the resemblance in both method and results is very close. The sound from an aeroplane travels too slowly to indicate the position of the source, and any radio signals it emits may be deliberately or inadvertently confusing to the observer, but an aircraft cannot avoid reflecting the radar pulse. In the brain, the spontaneous actions or thoughts which it initiates may be delayed, by a variable time, after the first electrical sign of their occurrence, and the spontaneous activity is usually too varied and uncontrollable to correlate with other physiological variables, but the central nervous system cannot escape the influence of external stimuli, since to respond to them is one of its prime functions. Moreover the stimuli can be given at moments controllable by the observer and at known frequencies.

By using techniques precisely similar to those developed for radar, the response to a regular stimulus can be displayed on a cathode-ray oscilloscope, so that scores of successive responses are precisely superimposed—whereas the random or spontaneous activity is blurred and unobtrusive. This method has been turned to great account by Dawson [1] in the study of the electrical responses to stimulation of sensory nerves in the limbs. Results of considerable general interest have been obtained by using rhythmic flashes of light for investigating the response-characteristics of the visual cortex [2], [3], [4]. When rhythmic stimulation of this sort is used, the frequency analyser already mentioned is of great value, since the regular responses at the stimulus frequency can be traced through the brain, even when they are smaller than the irregular background oscillations, because their steady recurrence is seen by the analyser as a prominent peak of activity at a single frequency.

This method has proved powerful in clinical applications, particularly when the resting records present no diagnostic features. In some epileptics, for example, it is possible to find a flash-frequency which sets up in the brain electrical activity which combines with the oscillations already present to produce a diagnostically abnormal pattern, and a clinical seizure. This observation, in combination with the known features of the spectrum of epileptic records, has suggested the hypothesis that the condition known as idiopathic epilepsy is due to the occasional synchronization by sensory or motor impulses of otherwise unrelated electrical rhythms. In cases with organic disease of the brain the response to rhythmic flashes of light is often disturbed near the site of a lesion, even when the resting activity appears normal.

In normal subjects, bright rhythmic flashes of light have been found to evoke peculiar sensations at certain frequencies. All subjects describe chequered, whirling patterns of light and shade when the stimulus frequency is between 7 and 30 flashes per second, and most see brilliant and ever-changing colours with white light. Some people, again, describe vivid hallucinations and dream-like experiences of flying or of distortion of the time sense. Most interestingly, whenever a peculiar sensation is experienced, some part of the brain displays at the same time an unusual and exaggerated degree of electrical activity at the frequency of the stimulus or a multiple of it. Furthermore, when,

ng an episode of this sort, the subject is uraged to submit to the sensation and to orce it with memories of a similar type, both ensation and its associated electrical discharge augmented. Conversely, when the subject stracted by another stimulus or, by an effort ill, refuses to accept the vision or state of mind iced by the stimulus, both the subjective and trical phenomena subside.

n some of the most striking examples of this ct, vivid and emotionally powerful feelings e been correlated with electrical responses in temporal and frontal lobes, not at the stimulus uency itself, but at harmonics of it. In general ns, complex individual mental disturbances be set up by an apparently neutral physiocal stimulus when this is rhythmic and powerenough, and these mental states are strictly related with electrical events in parts of the in which have nothing to do with the reception isual stimuli.

t will be recalled that unhappy children and l-tempered adults often show discharges at ut 6 cycles per second in the temporal lobes. is at least very suggestive that when similar ctrical discharges are evoked in normal people rhythmic stimulation, a feeling of emotional comfort and irritability appears. It would seem ical to adopt, as a working hypothesis, the ion that certain temperaments and states of nd are associated with electrical activity at a rticular frequency in certain nervous circuits hin the brain, and one can foresee a new aning of the word 'temper' as a strictly entific term to describe the tuning and resonance these circuits. In the testing of working hyposes 'the road of excess leads to the palace of dom,' and it may be necessary to develop a mplete theory of the relation between brain and nd in these electrical terms before the appearce of absurd conclusions or predictions signals inadequacy of our ideas. Even at the present e the introduction of electrical terms and alogies has accelerated advance, for it is now ssible to use the methods of electrical engineers the study of brain physiology. For example, en an engineer observes a sustained electrical oscillation he looks for what he calls 'positive feedback' and it seems likely that, in the brain, feedback circuits actually exist, and that their properties can be studied exactly as if the living organ were a complex transmission system. Going a step further, it has been found possible to construct models using devices similar to those postulated in the brain, and these models behave in a very lifelike fashion, particularly when positive and negative feedback circuits are combined. The positive feedbacks provide mechanisms for hunting, scanning, and testing the model's environment for stimuli and information, and the negative feedbacks or reflexes ensure that any action the model may decide to take will be as near as possible to that necessary for stability and survival. It is surprising how complex and apparently unpredictable the behaviour of one of these models can be when it is placed in the irregular environment of an ordinary room, even when it contains only half a dozen units as compared with the millions in the human brain.

The great fertility of the marriage between brain physiology and engineering has suggested to many people that the family of subjects thus united is worthy of a special name, and Wiener [5] has proposed 'cybernetics,' from the Greek word meaning 'steersmanship,' since the fundamental common problem seems to be the way in which complex dynamic systems direct themselves toward various goals. It has been predicted that when properly established this new branch of science may have as great an effect upon our life and surroundings as the achievements of nuclear physicists.

A comparison has already been made with the great calculating machines, but these are of course enormously more specialized than any viable living organism, since their sole function is to perform certain types of calculation at immense speed. In contrast to this, the brain performs innumerable functions, though none with very great accuracy or velocity—but it can design the machines. A good-quality human brain has more possibilities than any other known structure in the universe, and we should not be far wrong in calling it 'the universal machine.'

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Book reviews

THEORETICAL AND INORGANIC CHEMISTRY

A Text Book of Theoretical and Inorganic Chemistry, *by F. A. Philbrick and E. J. Holmyard. Revised in collaboration with W. G. Palmer. Pp. v + 835, with numerous line diagrams. J. M. Dent and Sons Limited, London.* 1949. 13*s.* 6*d. net.*

Seventeen years have elapsed since Philbrick and Holmyard's *Text Book of Theoretical and Inorganic Chemistry* first appeared. It has enjoyed wide popularity, and now the authors have prepared a new edition. The new work retains the general plan of the original text, but much of the matter has been rewritten to bring it into line with modern ideas and to incorporate recent advances in knowledge. As Mr Philbrick was unable to take an active part in the revision, Dr Holmyard secured the collaboration of Dr W. G. Palmer of Cambridge, whose valuable book on valency is well known to chemists. Part I serves as an excellent historical introduction, while Part II deals with general and theoretical chemistry. Here are discussed with lucidity and conciseness such topics as the structure of matter, the nature of solution, heterogeneous equilibrium and homogeneous equilibrium, electrochemistry and photochemistry, colloid and surface chemistry, radioactivity and atomic structure, and finally the theory of valency. In Part III the elements and their compounds are considered, the less common elements included. This new volume is admirably written and well illustrated, and bears evidence on every page of the hand of the experienced teacher. There is no doubt it will be even more successful than the original volume. Considering the size of the book and the attractive way in which it is produced the price is most reasonable. Candidates for pass and honours degrees and for university entrance scholarships should be sure to have this book. They will find it a good companion.

W. WARDLAW

ATMOSPHERIC ELECTRICITY

Atmospheric Electricity, *by J. Alan Chalmers. Pp.* 175, *with several line diagrams. Oxford University Press, London.* 1949. 15*s. net.*

Our knowledge of atmospheric electricity has been largely developed during the last fifty years by a band of enthusiasts, foremost amongst whom have been Elster and Geitel, C. T. R. Wilson, G. C. Simpson, and B. F. J. Schonland. Apart from a small monograph by the last named, no English text has been devoted to the subject. Dr Chalmers' book is claimed to fill this gap (wisely omitting the daughter subjects of ionospheric structure and cosmic rays, now quite beyond parental control), and to serve both as an introduction to the uninitiated and as a work of reference. This is difficult enough in 175 pages, but Dr Chalmers makes it quite impossible by assuming in his reader not even a knowledge of elementary electrostatics. He introduces laboured explanations involving lines of force for almost every application of Poisson's equation or Gauss's theorem, and is left with too little space for critical discussion of modern work.

The book's greatest value is as a source of references. Some 250 are listed, the majority being abstracted in the text. They carry the story up to 1947, apparently without important omission, except possibly of the recent work of J. Frenkel.

G. D. ROBINSON

REFLEX FACTORS

Conditioned Reflexes and Neuron Organization, *by Jerzy Konorski. Pp.* 267, *with* 18 *line diagrams. Cambridge University Press, Cambridge.* 1948. 18*s. net.*

This is an attempt to resolve highly integrated animal behaviour into reflex factors. Such resolution is extremely desirable, and the attempt is courageously conceived and executed. The field undertaken is the behaviour of the laboratory dog, and the observations proceed on the lines introduced by the great Russian observer, Ivan Pavlov, but the interpretation put upon them constitutes a great advance. Professor Konorski worked with Pavlov for a number of years, and after Pavlov's death continued independently the line of inquiry followed in the Leningrad Institute. The prosecution of patient scientific research was at the time of the preparation of this book in itself a notable achievement.

The observational basis of the work consists of the experiments due to Pavlov, and a long series of further ones by Professor Konorski and his Polish and Russian colleagues. These are now, in their English dress, made available to a fresh audience. It will be remembered that Pavlov expressed himself as not wholly satisfied with his own in pretation of some of the experime results he obtained. Particularly his later years, his explanations ha call in what he called the differ 'temperaments' for some of his ind dual dogs. Professor Konorski rew ing over the subject now furnishes amended and more strictly phy logical explanation of the 'conditio reflex' as exemplified. This type animal 'behaviour,' if we go back to Hughlings Jackson paradigm, is reaction belonging to the highest t of the three Jacksonian levels. It is c mingled therefore with the mental the psychical. That is a welcome about it today, because it is precis that type of behaviour which has, regards experimental inquiry, rather in a backwater in recent ye In Europe, though less in America has suffered from falling between stools, neurology and psychology. P fessor Konorski is to be congratula on his valuable monograph.

C. S. SHERRINGT

A HISTORY OF THE ROYAL SOCIETY

Scientists and Amateurs, *by Doro Stimson. Pp. xiii* + 270. *Sigma Bo Limited, London.* 1949. 15*s. net.*

The author, who is chairman of t history department at Boucher Colle Baltimore, states in her preface: 'Tho who have the time and the opportuni to look through the Royal Society's ov *Record* or to refer to its treasure recent careful study of its administr tion for nearly three centuries may n need this book. But copies of neith book are readily available to American public because of cost scarcity, nor is either one planned the general reader who knows little nothing of the Royal Society at t outset.'

Miss Stimson has succeeded admirab in this attempt to interest the gener reader in the life-story of one of th world's oldest scientific bodies. Her boo is scholarly, authoritative, and compre hensive; its style is excellently adapte to its object; its illustrations are wel chosen and beautifully reproduced Scientists and amateurs alike wil discover that this is a volume difficul not to finish at one sitting; the British as well as the American, public will find it full of fascination.

JAMES KENDALL